Research Governance and Site Specific Assessment

Process and Practice

VICTORIA State Government | Department of Health

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1 Definitions

Abbreviation	Definition
ABN	Australian Business Number
AE	Adverse Event
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
ARTG	Australian Register of Therapeutic Goods
AUD	Australian Dollar
CEO	Chief Executive Officer
CIRA	Clinical Investigation Research Agreement
CPI	Coordinating Principal Investigator
CRA	Contract Research Associate (also known as 'monitor')
CRO	Contract Research Organisation
CTA	Clinical Trial Approval
CTN	Clinical Trial Notification
CTRA	Clinical Trial Research Agreement
CV	Curriculum Vitae
DIR	Dealing Involving Intentional Release (of a GMO into the environment)
DNIR	Dealing Not Involving Intentional Release (of a GMO into the environment)
ERM	Ethical Review Manager
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practice
GMO	Genetically Modified Organism
GST	Goods and Services Tax
HREC	Human Research Ethics Committee
IB	Investigator Brochure
IBC	Institutional Biosafety Committee
ICH-GCP	International Conference on Harmonisation – Good Clinical Practice
IFU	Instructions for Use
IND	Investigational New Drug
MA	Medicines Australia
MDF	Minimal Dataset Form
MTAA	Medical Technology Association of Australia

Abbreviation	Definition
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
OGTR	Office of the Gene Technology Regulator
PI	Principal Investigator
PICF	Participant Information Consent Form
RGO	Research Governance Officer
SEBS	Southern Eastern Border States
SOC	Standard of Care
SSA	Site Specific Assessment
SSI	Significant Safety Issue
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration
USADE	Unanticipated Serious Adverse Device Effect
VHIMS	Victorian Health Incident Management System
VMIA	Victorian Managed Insurance Authority
VSM	Victorian Specific Module

2 Resources

Clinical trials and research
www.clinicaltrialsandresearch.vic.gov.au

National Mutual Acceptance
www.clinicaltrialsandresearch.vic.gov.au/national-mutual-acceptance

Research Governance Checklist
Download at www.clinicaltrialsandresearch.vic.gov.au/research-governance-applications

Roles and Responsibilities in a Research Project
Download at www.clinicaltrialsandresearch.vic.gov.au/ethics-application

ERM for **applicants** (investigator, trial coordinator, sponsor/CRO)
https://au.forms.ethicalreviewmanager.com/

ERM training for applicants (investigator, trial coordinator, sponsor/CRO)
www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager

Applicant User Guide to ERM
Download at www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager

ERM for **research offices**
https://vic.review.ethicalreviewmanager.com/

ERM training for research offices
Email multisite.ethics@health.vic.gov.au

National teletrials compendium
www.health.gov.au/resources/collections/the-national-teletrials-compendium

CTN and CTA
www.tga.gov.au/clinical-trials

VMIA clinical trials guide
www.vmia.vic.gov.au/~/media/internet/content-documents/risk/guides-and-publications/clinical-trials/clinical-trials-guide.pdf

Safety and breach monitoring and reporting
www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods

Australian Code for the Responsible Conduct of Research
www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018

National Statement on Ethical Conduct in Human Research
www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

National Clinical Trials Governance Framework
www.safetyandquality.gov.au/standards/national-clinical-trials-governance-framework

3 Introduction

This document, Research Governance and *Site Specific Assessment Process and Practice*:

- Provides guidance to assist all sectors involved in clinical trials and research to understand the processes for meeting regulatory requirements in Australia
- Refers to research governance/site-specific assessment (SSA), as it is site assessment that is central to governance of the regulatory aspects of research
- Contains information relevant to all types of human health and medical research, although some references apply to clinical trials only
- Relates specifically to research governance/SSA at sites in **Victoria**; some information may be utilised for sites in other states/territories, if appropriate
- Describes best-practice processes for research governance/SSA; the actual steps and timing may vary as they depend on the management at individual institutions
- Contains information for investigators/trial coordinators, RGOs and sponsors/CROs. All parties should review each section to gain a better understanding of each other's roles and responsibilities.

Research governance/SSA

Research governance can be defined as the broad range of regulations, principles and standards of good practice that exist to achieve, and continuously improve, research quality across all aspects of healthcare. This document refers to how the research is conducted at a site and, as such, covers a wide range of considerations.

Components of research governance include:

- **Ethical protection of participants** – dignity, rights, safety and wellbeing
- **Scientific integrity** – high-quality, valid research
- **Health and safety** – occupational health and safety and physical, legal and social issues, e.g. where the research is undertaken and the experience of the research team
- **Information** – public access to information and findings; the role of the complaints contact person, whether they are suitable and have sufficient time
- **Business** – accountabilities and responsibilities, e.g. compliance with legal requirements, correct contractual arrangements and robust budget management
- **Quality research culture** – promotion of excellence

The SSA form is the core document to manage the requirements of site governance assessment. The SSA form holds the information on how the project will be conducted at the site; it includes supporting documentation and essential signatures.

3.1 Ethics and research governance/SSA

There are two regulatory components required before a research project can commence at a site in Victoria – ethics approval and research governance/SSA authorisation. This document describes processes for research governance/SSA. Information on ethics is at www.clinicaltrialsandresearch.vic.gov.au/ethics-application.

Terminology: The HREC 'approves' a project; the research governance/SSA process 'authorises' the site to proceed with the research. The RGO 'acknowledges' (accepts) the advice or decision of the reviewing HREC.

Differences between ethics and research governance/SSA

Ethics	Research Governance/SSA
• Reviewed by Human Research Ethics Committee (HREC)	• Reviewed by site Research Governance Officer (RGO
• Considers ethical aspects of clinical trial or research	• Considers risk management, law, strategic alignment, finance, resources, management of research at site
• Coordinating Principal Investigator (CPI) is responsible for application, communications and reporting	• Site Principal Investigator (PI) is responsible for application, communications and reporting
• Occurs once for a multi-site research project	• Occurs separately at every site participating in a multi-site research project
• Undertaken at any organisation accredited under National Mutual Acceptance (NMA)	• Undertaken at the specific site where the research project is conducted
• Any delay impacts the SSA review	• Authorisation is dependent on ethics approval being granted

It is recommended that ethics and research governance/SSA processes occur in parallel. Research governance/SSA authorisation is granted **after** ethics approval, but commencing the research governance/SSA process early ensures there are minimal delays and authorisation can occur as soon as possible after approval. When SSA authorisation is given, the research project can commence at the site.

A single-site research project (taking place at one health service or institution) requires HREC approval and research governance/SSA authorisation.

A multi-site research project (taking place at more than one health service or institution) requires one HREC approval that covers all sites, and every site requires its own research governance/SSA authorisation.

3.1.1 Streamlining clinical trials and research

The Victorian streamlined framework enables one ethics approval no matter how many sites participate in a multicentre clinical trial or research project. The reviewing HREC is responsible for the ethical and scientific review of the research project for all participating sites. In addition to the **single ethical approval**, each participating site must undergo its own **research governance/SSA process to ensure institutional oversight**, which takes into account the appropriateness of the research at the site and whether the institution has the resources and facilities to conduct the project.

The primary focus of the streamlined system is to achieve timely and efficient research governance authorisation for multi-site research projects so they can commence as quickly and safely as possible. This benefits patients by allowing them to receive new treatments sooner, and improves Victoria's competitiveness in attracting global research projects.

3.1.2 National Mutual Acceptance

Victoria collaborates with other Australian states/territories in National Mutual Acceptance (NMA), a national system for mutual acceptance of scientific and ethical review of multi-centre human research projects conducted in publicly funded health services across jurisdictions.

A multi-site research project taking place in multiple NMA states/territories undergoes a single ethical review. Research governance/SSA is required at each site.

Full information on NMA is at www.clinicaltrialsandresearch.vic.gov.au/national-mutual-acceptance.

3.1.3 Commercially sponsored research projects

Throughout this document, the sponsor and Contract Research Organisation (CRO) are referred to together. 'Sponsor/CRO' encompasses related personnel.

Following feasibility and site selection for a clinical trial there are specific tasks required of the sponsor/CRO, and negotiation of additional assistance may be agreed. As a sponsor/CRO, communication with clinical trial site personnel is essential to ascertain local site requirements for research governance/SSA. This document provides information to ensure a streamlined approach is achieved among all parties.

3.1.4 Summary of processes

Before ethics application

- In ERM, CPI/trial coordinator (or sponsor/CRO) gives site PI/trial coordinator access to SSA and visibility of ethics application or MDF
- Site PI/trial coordinator:
  - liaises with site RGO
  - obtains site documents from sponsor/CRO (e.g. legal documents)
  - completes SSA form in ERM and uploads supporting documents

After ethics application submitted

- Site PI/trial coordinator submits SSA
- RGO reviews submission and, as required, requests additional information/documents
- Site PI/trial coordinator may liaise with CPI/trial coordinator or sponsor/CRO to obtain information; they should respond promptly
- Site PI/trial coordinator edits application and submits response to RGO's requests

After ethics approval

- CPI trial coordinator informs site PI/trial coordinator of approval
- Site PI/trial coordinator resubmits SSA with ethics approval letter/certificate uploaded
- RGO views approved ethics documents in ERM and reviews SSA submission; may request additional information/documents for SSA
- Site PI may liaise with CPI or sponsor/CRO to obtain requested information; they should respond promptly
- Site PI/trial coordinator edits application and submits response to RGO's requests
- RGO completes final review and when all is finalised, authorises SSA
- RGO notifies site PI/trial coordinator of SSA authorisation

Conduct of project

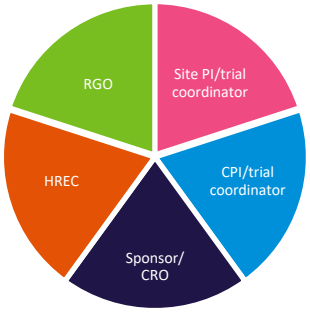
- Amendments: After HREC amendment approval, PI submits *Site Governance Amendment* to notify RGO of HREC amendment approval; RGO considers impact on site and authorises amendment at site.
- Safety issues: HREC acknowledges; PI notifies RGO who considers impact on site
- Progress reports: HREC acknowledges *Project Progress Report*; PI submits *Site Progress Report* to RGO; RGO considers impact on site and acknowledges site progress report

Closure of project or site

- CPI notifies reviewing HREC
- HREC acknowledges receipt. If project closed at all sites, HREC closes ERM ethics record
- PI notifies RGO
- RGO acknowledges receipt and closes ERM research governance/SSA record

3.2 Communication

Key stakeholders in research governance/SSA



Both before and after approval and authorisation, it is essential to ensure good communication among all parties involved in the research project. Open lines of communication should be established from the inception of the research proposal – discussing and coordinating processes from the start paves the way for efficient regulatory processes.

All contributors to the regulatory steps required for research should familiarise themselves with the processes and practices outlined in this document. Consistency within the research governance process is important, and establishing uniform practices enables timely processing.

In the event of the HREC requesting information from the CPI, or the RGO requesting information from the PI, providing a timely response is crucial to avoid a delay in commencing the research project.

- Site PI/trial coordinator works collaboratively with the sponsor/CRO and the site RGO.
- RGO liaises with relevant stakeholders to agree on roles and information to be provided by the site PI.
- Sponsor/CRO communicates with site clinical and research team concerning local site requirements for research governance/SSA.

Collaboration between all parties is paramount, and good communication will underpin resolution of any issues that may arise.

3.3 ERM

Ethical Review Manager (ERM) is used for all ethics and research governance applications in Victoria and Queensland. ERM is a complete management system for governance processes, and is used by investigators/trial coordinators, RGOs, sponsors/CROs and reviewing HRECs.

All those involved with research governance processes should have their own ERM account. They should be familiar with its features and refer to the Applicant User Guide to ERM. ERM information and training are at www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager.
A process overview is in Appendix 1 and Appendix 2.

It is recommended that the sponsor/CRO and investigators/trial coordinators establish ERM responsibilities as early as possible. Using ERM is an efficient way to share documents with sites, and the research team must be aware of who is managing aspects of the application in ERM. Appendix 3 can be used to facilitate this.

The CPI is responsible for completion and submission of the ethics application form in ERM, and a SSA form for each site is created as a sub-form of the main ethics form. The site PI is responsible for completion and submission of their own site's SSA.

If the ethics review takes place in a NMA state/territory that does not use ERM, then a proxy form is created in ERM to allow SSAs to be created for Victorian and Queensland sites. The proxy form is known as the Minimal Dataset Form (MDF) – it is **not** an ethics application form, but allows ethics documents to be shared with sites and RGOs. For MDF guidance refer to Section 11 of the Applicant User Guide to ERM.

Information on SSAs for other states/territories (ACT, NSW, NT, SA, Tas, WA) is at www.clinicaltrialsandresearch.vic.gov.au/national-mutual-acceptance.

3.4 TGA requirements for clinical trials

The Therapeutics Goods Administration (TGA) administers the Clinical Trials Notification (CTN) and Clinical Trials Approval (CTA) schemes. These provide an avenue for 'unapproved' therapeutic goods to be lawfully supplied for use solely for experimental purposes in humans. Information is at www.tga.gov.au/clinical-trials. The CTN scheme is a notification process where the Australian clinical trial sponsor must notify the TGA of the intent to sponsor a clinical trial involving an 'unapproved' therapeutic good. The CTA route is generally used for high-risk or novel treatments where there is no or limited knowledge of safety.

A clinical trial involving unapproved therapeutic goods must go through either the CTN or CTA scheme, and evidence must be provided to the RGO as part of the research governance/SSA process.

The sponsor/CRO is responsible for CTN or CTA submission to the TGA. Where an institution is acting as sponsor, the institution is responsible for actioning this; the process may be overseen by the institution's RGO.

3.5 Research agreements

The research agreement is a crucial aspect of research governance/SSA. It is a legal document between the institution and sponsor/CRO which agrees the terms of conducting the project at the site.

It is recommended that all research projects use a standard template for their research agreements. The appropriate template should be used for the type of research project. Medicines Australia (MA) and the Medical Technology Association of Australia (MTAA) have produced templates for the Clinical Trial Research Agreement (CTRA) and Clinical Investigation Research Agreements (CIRA) respectively.

Clinical trial of a drug

Medicines Australia represents the discovery-driven pharmaceutical industry in Australia. Australian institutions accept the Medicines Australia agreed CTRA templates:

- CTRA – Medicines Australia Standard Form
- CTRA – Contract Research Organisation acting as the local sponsor
- CTRA – Collaborative or Cooperative Research Group (CRG) studies
- CTRA – Phase 4 clinical trial (medicines)
- CTRA – Phase 4 clinical trial (medicines) Contract Research Organisation acting as the local sponsor
- CTRA subcontract for studies conducted under a tele-trials model – Agreement between the primary site and satellite site. Required for each satellite site, in addition to the CTRA (head agreement) between the sponsor and primary site.

CTRA templates and guidance are at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements.

Clinical trial of a medical device

The MTAA is the national association representing companies in the medical technology industry. An important distinction between investigation agreements developed for the pharmaceutical and the medical technology industries is the use of the international standard ISO 14155:2003 Parts 1 and 2 for the study of medical technology. The MTAA's template CIRAs reference this standard.

- MTAA Standard CIRA
- MTAA Standard CIRA Post Market
- MTAA CIRA: Contract Research Organisation acting as the Local Sponsor
- MTAA CIRA: Post Market Clinical Trial (Medical Devices) – Contract Research Organisation acting as Local Sponsor.

CIRA templates and guidance are at www.mtaa.org.au/clinical-investigation-research-agreements.

Investigator initiated clinical trial

A CTRA for investigator initiated research is available for use at sites in Victoria only; it was developed by the Victorian Managed Insurance Authority (VMIA). Additional conditions may be added in Schedule 4, and it is at the discretion of the institution whether the schedule requires legal review. The investigator initiated CTRA is at www.clinicaltrialsandresearch.vic.gov.au/research-governance-applications.

Special conditions and non-standard agreements

Wherever possible, a standard template should be used. It is not acceptable for changes to be made to clauses in the body of a standard research agreement. A schedule for 'Special conditions' in each of the agreements allows limited customisation for company, study-specific or institutional purposes. Special conditions may be added to a CTRA or CIRA in either Schedule 4 or Schedule 7, depending on the template, with endorsement through the Southern Eastern Border States (SEBS) panel. SEBS is a collaborative initiative among jurisdictions and consists of representatives from New South Wales, Queensland, South Australia, Tasmania and Victoria.

It is a sponsor/CRO responsibility to ensure SEBS endorsement of any special conditions added to Schedule 4 or 7, prior to submitting the research agreement to RGO for review.

Guidance on submitting a request to SEBS, including the *SEBS Review Template*, is at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/ (medicines) and www.mtaa.org.au/clinical-investigation-research-agreements (medical devices).

The SEBS panel meets monthly and reviews the proposed additions to the standard research agreements for medicines and devices. Each SEBS member state individually notifies the sponsor/CRO of endorsement, and securely shares all agreed schedules with RGOs in their jurisdiction as a reference for review of CTRAs.

Some institutions do not accept non-standard agreements but, if accepted, the recommended practice is that local legal review is sought for any non-standard agreement. The format of non-standard agreements is diverse. The sponsor/CRO is responsible to pay for legal review and should be informed before the legal review is conducted.

The sponsor/CRO should use a standard CTRA (medicines) or CIRA (devices) to eliminate the need for legal review at each site and to minimise legal costs to industry companies.

3.6 Teletrials

A teletrial uses telehealth technology to communicate between the Primary Site and Satellite Site/s and enable delivery of aspects of a clinical trial as defined in the Supervision Plan. This technology supports a Principal Investigator to supervise Associate Investigator/s to conduct a clinical trial at a Satellite Site which is geographically remote from the Principal Investigator's Primary Site. The Principal Investigator remains responsible for the trial.

Guidance for teletrials in Victoria is at www.clinicaltrialsandresearch.vic.gov.au/ethics-application. The *National Teletrials Compendium* is at www.health.gov.au/resources/collections/the-national-teletrials-compendium. The compendium consists of the *National Standard Operating Procedures for Clinical Trials, including Teletrials in Australia* and the *National Principles for Teletrials in Australia*.

The teletrials process for research governance/SSA is similar to that of a standard research project, but additional documents are required:

- Standard CTRA Teletrial Subcontract (between Primary site and Satellite site) for each Satellite site (accessible at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements)
- Supervision Plan (between Primary site and Satellite site) for each Satellite site (template is in the *National Standard Operating Procedures for Clinical Trials, including Teletrials in Australia*)

A Supervision Plan outlines processes for a Principal Investigator in the supervision of any individual or party to whom he/she delegates study-related duties and functions conducted at a Satellite Site. This includes, but is not limited to, details on joint consultations using telehealth, collation and monitoring of documents, frequency of joint trial meetings across a cluster (with minutes of these meetings) and clarification of activities performed by the PI and the AI, other study staff and independent third party i.e. external service providers.

3.7 Research involving ionising radiation

Procedures that involve ionising radiation include diagnostic imaging and nuclear medicine scans. If a research project involves exposing participants to ionising radiation, there are specific requirements for both ethics and research governance/SSA, to ensure ethical protection and safety of participants.

The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) develops codes, standards, guides and provides advice. The *Radiation Protection Series No. 8 Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes* ensures researchers provide radiation exposure information that allows consent to be properly considered by participants and the HREC. There can be issues applying the *Code* to multi-centre research, and the ARPANSA Radiation Health Committee has issued a Statement on ethical review for multi-centre trials.

Appendix 4 provides information on regulatory requirements and supporting documents.

At site selection, the sponsor/CRO must survey participating sites to determine whether the protocol's ionising radiation level is **standard of care** or **additional to standard of care** at each site. If a new site is later added via amendment, the sponsor should also survey that site. The ethics and research governance/SSA processes depend on whether participants will receive a level of ionising radiation that is **part of** standard clinical care, or a level that is **additional to** standard clinical care.

Ethics and governance processes for ionising radiation in research

Level of ionising radiation	Ethics: single-site project	Ethics: multi-site project	Research governance/SSA
None	N/A	N/A	N/A
Part of standard clinical care	• Site PI completes letter and uploads it as a supporting document in the ethics application. • Site PI submits ethics application. • HREC reviews documents.	• Each site PI completes letter and provides it to the CPI. • CPI uploads site letters as supporting documents in the ethics application. • CPI submits ethics application. • HREC reviews documents.	• Site PI submits research governance application. • RGO has access to ethics supporting documents and reviews the site letter.
Additional to standard clinical care	• Medical Physicist completes an independent assessment report. • Site PI uploads the Medical Physicist's report as a supporting document in the ethics application. • Site PI submits ethics application. • HREC reviews documents.	• At each site, a Medical Physicist completes an independent assessment report. • Depending on reviewing HREC's policy, ***either***: CPI uploads **all** site assessment reports as supporting documents in the ethics application. ***or*** CPI uploads **one** assessment report (from the site with the highest assessed dose) as a supporting document in the ethics application. • CPI submits ethics application. • HREC reviews documents.	RGO has access to the ethics supporting documents, so process depends on documents included in ethics application. • *For a multi-site research project where only **one** Medical Physicist report was uploaded to the ethics application:* Site PI uploads the site Medical Physicist's report as a supporting document in the research governance/SSA application. • Site PI submits research governance application. • RGO reviews documents (site radiation safety risk assessment and ethics approval letter). • For details see Section 5.2.2.2.

The Victorian Department of Health (DH) licenses users of radiation sources under the *Radiation Act 2005*.

Reporting requirements for ionising radiation in research

Radiation dose	Action required
Above dose constraint of ARPANSA Code	The institution (licence holder) must notify Radiation Team at DH. The RGO may action the DH notification, or verify that it has been done by another party. The project may commence prior to notification.
Below dose constraint of ARPANSA Code	DH notification is not required.

3.8 Post-authorisation monitoring and reporting

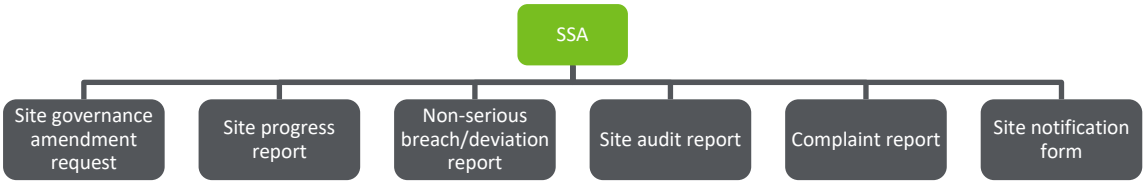
For the duration of an approved research project, the reviewing HREC is responsible for monitoring the ethical conduct and safety of the research; this is done via **post-approval** reporting. The site RGO is responsible for monitoring the conduct of the research project at their site via **post-authorisation** reporting. The CPI and site PI have ongoing responsibilities to report to the HREC and RGO respectively. Information on monitoring and reporting is at www.clinicaltrialsandresearch.vic.gov.au/monitoring-and-reporting.

Reporting to the HREC and RGO is generally the responsibility of investigators, but the sponsor/CRO can assist with creating and completing reports as appropriate. The responsibilities for reporting should be established at the inception of the research project (see Appendix 3).

Post approval reporting includes: ethics amendment, safety event, annual safety, serious breach, suspected breach, project progress, project final, site closure (one site closing from a multi-site project).

Post authorisation reporting includes: site governance amendment, non-serious breach/deviation, site progress, site audit, complaint, site notification. The site notification form is used to inform the RGO of post-approval reports sent to HREC, or any other site reporting for which there is not a dedicated form.

Post-authorisation report forms from SSA



Monitoring and reporting must align with the NHMRC guidance *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* and *Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods*.

Safety events to be reported

Event	Description
Significant Safety Issue (SSI)	A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	An adverse reaction that is both serious and unexpected.
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Breaches to be reported

Type	Description
Serious breach	A breach of Good Clinical Practice (GCP) or the protocol that is likely to affect to a significant degree the safety or rights of a research participant or the reliability and robustness of the data generated in the research project.
Suspected breach	A report that is judged by the reporter as a possible serious breach but has yet to be formally confirmed as a serious breach by the sponsor.

Institutional guidance on safety events and breaches

An institution may publish its own safety monitoring and reporting guidelines that reference the NHMRC guidelines and incorporate other considerations, such as incident reporting. An institution may require all safety incidents with ‘site impact’ to be reported to their RGO. **Parties must adhere to the institution’s policy on safety reporting**.

4 Investigators and trial coordinators

4.1 Getting started

For information on investigator duties, see the Roles and Responsibilities in a Research Project at www.clinicaltrialsandresearch.vic.gov.au/ethics-application.

4.1.1 Coordinating Principal Investigator (CPI) preparation

Once site selection has occurred the CPI/trial coordinator, in collaboration with the sponsor, identifies key personnel involved in research governance for the project, including:

- the PI/trial coordinator at each participating site
- the RGO at each participating site
- the monitor/CRA.

A meeting with each of the parties should be held so all are informed of the requirements for the SSA submission. It should be confirmed that all parties have access to ERM for sites in Victoria or Queensland, and other software systems for sites in other states/territories.

The research governance/SSA process should occur in parallel with the ethics review – early action facilitates timely review and authorisation.

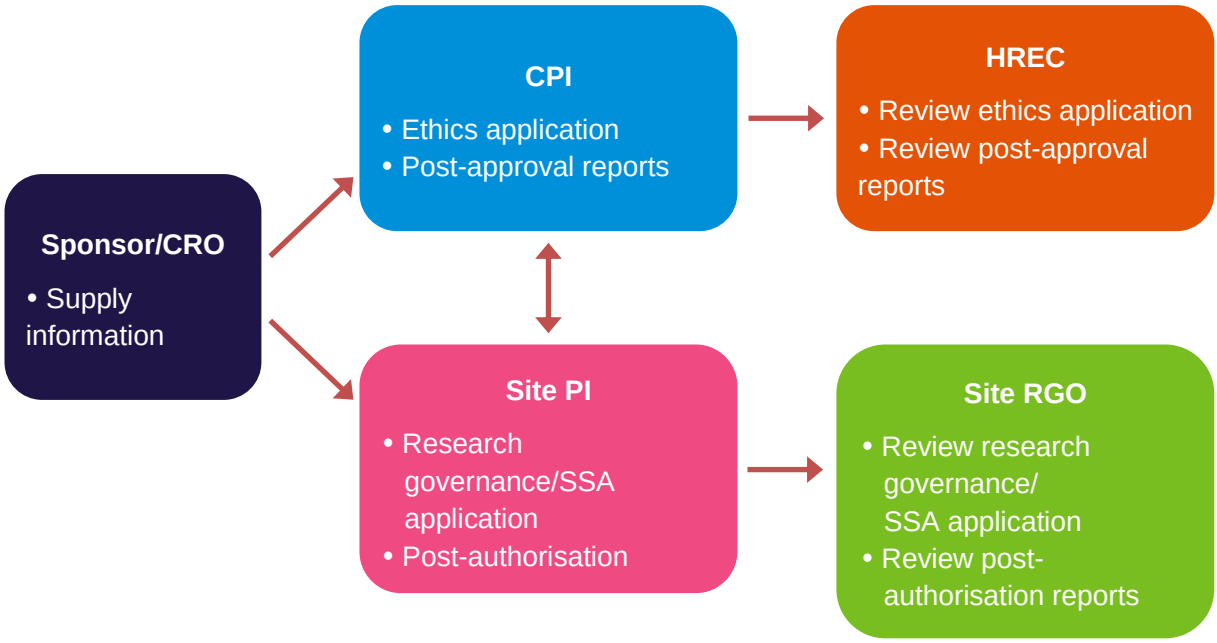
The research governance process should begin as soon as site selection occurs. To facilitate research governance at sites, the CPI/trial coordinator must ensure each site PI/trial coordinator has:

- All supporting documents necessary for the research governance/SSA application (see Research Governance Checklist)
- Access to their own site's SSA form (for Victoria refer to Section 9 of the Applicant User Guide to ERM)
- Visibility of the ethics application form and its supporting documents (for Victoria this is managed in ERM).

4.1.2 CPI communications with sites

The CPI is responsible for the ethics application. Communication between the CPI and reviewing HREC must be timely to avoid delaying ethics approval and SSA authorisations.

The CPI is also responsible for communicating information about the ethics application and approval to each site PI/trial coordinator; this should be done promptly to allow each site to progress their research governance/SSA application.



The CPI for a multi-site research project may use a contact template (Appendix 5) to record project details and participating site information. It can be sent to the sponsor to complete initially, and then be maintained throughout the project by the CPI. The template is a reference to ensure all relevant personnel are listed and included in communications. It is the responsibility of the sponsor and/or site PI to inform the CPI of any staffing changes throughout the study, so the template can be updated accordingly.

Tracking the progress of the ethics and research governance/SSA applications from submission to approval/authorisation can be managed efficiently in ERM using the History and Submissions tabs. Refer to Section 2.7 of the Applicant User Guide to ERM.

Tip: For Victoria and Queensland sites, an efficient communication tool is to give each site PI and trial coordinator an appropriate ERM role from the ethics application form (for Victoria, refer to Section 3.5 or 7.4 of the Applicant User Guide to ERM).

4.1.3 Principal Investigator (PI) participating site preparation

Each site PI/trial coordinator must keep in contact with the CPI, who is responsible for relaying ethics communications to the sites. The sponsor provides the CPI with each participating site's contact details, enabling the flow of information to sites. Any staff change at the participating site should be communicated to the sponsor who informs the CPI.

The research governance process should begin as early as possible. The PI is encouraged to discuss their intention to conduct a research project early with their manager and Head of Department to seek their support; at this time they can also ensure the Head of Department has an ERM account.

To begin research governance/SSA, the PI/trial coordinator must ensure they have:

- All supporting documents necessary for the research governance/SSA application (see Research Governance Checklist)
- Access to their own site's SSA form in ERM (this is facilitated by the CPI/trial coordinator)
- Visibility of the ethics application form and its supporting documents in ERM (this is facilitated by the CPI/trial coordinator).

Members of the site research team should each have their own ERM account. The PI/trial coordinator must be made aware of the email address that each team member uses for ERM login, in order to facilitate use of the system. ERM training information is at www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager.

The PI/trial coordinator should verify SSA form signatories (e.g. Head of department) each have their own ERM account and are familiar with the process for electronic signature (see Section 9.5 of the Applicant User Guide to ERM). The PI/trial coordinator must be made aware of the email address that each signatory uses for their ERM account, in order to make requests in the system.

The PI/trial coordinator should familiarise themselves with the reporting requirements of both the reviewing HREC and their institution's RGO (e.g. reporting safety event or serious breach).

Tracking the progress of the research governance/SSA application from submission to authorisation can be managed efficiently in ERM using the History and Submissions tabs. Refer to Section 2.7 of the Applicant User Guide to ERM).

4.2 Research governance/SSA application

4.2.1 Preparation

The CPI is responsible for submitting the ethics application to the reviewing HREC. For information on ethics application process, refer to www.clinicaltrialsandresearch.vic.gov.au/ethics-application.

The research governance/SSA process should occur in parallel with the ethics review – early action facilitates timely review and authorisation.

The research governance/SSA process can begin when the sponsor/CRO provides key documents to the CPI/trial coordinator. The CPI should receive from the sponsor/CRO:

- Protocol
- Investigator brochure
- Other ethics supporting documents e.g. Master PICF
- Medicines Australia form of indemnity for clinical trial HREC review and conduct of the trial for each participating site
- Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme for each site, if applicable.
- Research agreement

The above documents must be distributed to participating sites. Depending on the agreed delegations for the project, the documents are distributed by either the CPI/trial coordinator or the sponsor/CRO. For sites in Victoria and Queensland, the site PI/trial coordinator can view ethics documents in ERM (if given appropriate ERM role).

The sponsor/CRO should provide each participating site with a complete package of site documents. Using a package is preferred to avoid confusion. Timely provision of documents is important; it allows time for the site to prepare. Participating sites should receive:

- Medicines Australia form of indemnity for clinical trials: standard
- Clinical trial research agreement (CTRA) *or* Clinical investigation research agreement (CIRA)
- Detailed budget (may be a draft)
- Research governance fee

- Evidence of CTN.

The site PI/trial coordinator must check the correct company name, address, financial and other contact details appear on documents. Inconsistencies can delay the research governance/SSA process.

To expedite the governance process it is advised to simultaneously arrange for completion of the FDA 1572 Statement of Investigator form (this must be signed before beginning participation in a clinical study conducted under the Investigational New Drugs (IND) regulations), including financial disclosures and curriculum vitae (CV), where applicable.

4.2.2 ERM and SSA

ERM (https://au.forms.ethicalreviewmanager.com) is used for all ethics and research governance applications in Victoria and Queensland. The CPI is responsible for completion and submission of the ethics application form in ERM, and a SSA form for each site is created as a sub-form of the main ethics form. The site PI completes and submits their own SSA.

The creation and management of SSAs in ERM is determined by the CPI/trial coordinator and sponsor/CRO. They can either create SSAs themself and give full access to the site's PI, or give the site PI permission to create their own SSA (refer to Section 9 of the Applicant User Guide to ERM). The CPI/trial coordinator must ensure each site's PI is able to view the ethics application form (or MDF) and its supporting documents in ERM.

In ERM, the site PI is responsible for completing the SSA form, uploading supporting documents and submitting to the site RGO. The PI can give members of the site research team permissions to collaborate on the form; each person requires their own ERM account.

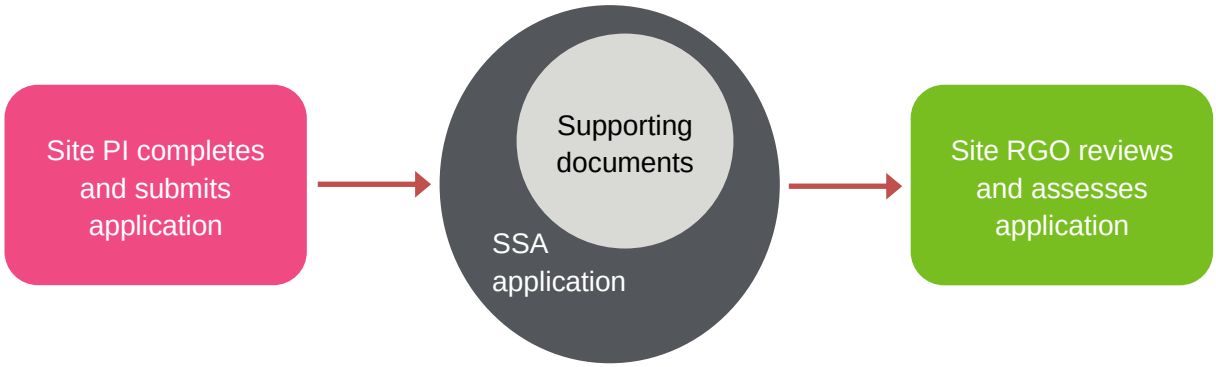
It is the responsibility of the CPI to upload *ethics* supporting documents in ERM. Ethics documents should not be uploaded in the SSA; only site research governance/SSA supporting documents should be uploaded. The RGO has visibility of the ethics documents in ERM.

The SSA form must be signed by the PI and associate investigators, as well as departmental heads. Each signatory must have their own ERM account in order to sign electronically. For efficiency, signatures should be requested concurrently. It is essential that the form and its uploaded documents are complete before signing, as any changes will invalidate signatures that have been applied. For SSA signature guidance refer to Section 9 of the Applicant User Guide to ERM.

4.2.3 Submission

It is recommended to submit the SSA early to allow the RGO time to review documents. The SSA can be submitted as soon as the ethics application has been submitted to the reviewing HREC.

The PI/trial coordinator uses ERM to submit the signed SSA and supporting documents to the site RGO. The RGO then uses ERM to review the application and request additional information, if required.



If the SSA is submitted before ethics approval has been granted (the recommended course), the RGO requests additional information to allow the PI to upload and submit the ethics approval letter.

In response to a request from the RGO, the PI/trial coordinator edits the SSA form and/or uploads supporting documents and then re-submits to the RGO (refer to Section 10 of the Applicant User Guide to ERM). Particular attention should be paid to version control and proper upload of supporting documents in the SSA, to ensure the correct documents are viewed and authorised by the RGO. A response to the RGO must be provided in a timely manner to ensure efficient review of the SSA. It is at the RGO's discretion whether the SSA is required to be signed again.

Only *current* versions of supporting documents must be included in the SSA submission, any superseded document versions must be removed before submission. Document versions are listed on the research governance/SSA authorisation letter, and so version control is of prime importance.

4.2.4 Authorisation

When the RGO is satisfied that the SSA application meets all requirements, the RGO facilitates Institution executive signature on the research agreement. The RGO then authorises the SSA and notifies the site PI/trial coordinator. The authorisation letter may include conditions of authorisation; the PI should pay particular attention to the conditions and ensure all obligations are met.

The PI must notify the CPI and sponsor/CRO of authorisation (or, if given appropriate permission, the CPI and sponsor/CRO can view the authorisation information in ERM).

For the duration of the project, the site PI (and the CPI) are responsible for providing the RGO with all relevant amendments, safety issues, and any information relevant to the conduct of the project in a timely manner, as they occur.

4.3 During the research project

For the duration of an approved research project, the reviewing HREC is responsible for monitoring the ethical conduct and safety of the research. The site RGO is responsible for monitoring the conduct of the research project at a site. The CPI and site PI have ongoing responsibilities to report to the HREC and RGO respectively.

Information on reporting is at www.clinicaltrialsandresearch.vic.gov.au/monitoring-and-reporting.

Reporting to a Victorian site RGO is managed in ERM; see Section 15 of the Applicant User Guide to ERM and Appendix 2.

Reporting should align with the National Health and Medical Research Council (NHMRC) guidance *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*.

Reporting to the HREC and RGO is the responsibility of investigators, but the sponsor/CRO can assist with creating and completing reports as appropriate. The balance of reporting responsibilities should be established at the inception of the research project; Appendix 3 can be used to facilitate this. Use the collaboration features of ERM for efficiency in reporting processes.

4.3.1 Amendments

An amendment is a written change to an HREC-approved protocol for ongoing research. An amendment may have a minor or a substantial impact on research governance/SSA at the site. If the research team is unsure about an amendment, the CPI should consult the reviewing HREC's research office, or the site PI should contact their RGO.

4.3.1.1 Notify the RGO of an ethics amendment

The CPI/trial coordinator is responsible for submitting an amendment request to the reviewing HREC. For a HREC in Victoria, an *Ethics Amendment Request* form is created as a sub-form of the HREA in ERM. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for approval.

The CPI must notify participating site PIs of the ethics amendment and its approval; they may do this directly or via the sponsor/CRO. The communication preference should be clearly established with the sponsor/CRO at the beginning of the research project, to ensure all relevant HREC-related information and correspondence is distributed to participating sites.

Any change to the ethically approved project can impact SSA authorisation, and so the RGO must be notified in a timely manner.

When the site PI/trial coordinator receives information about an ethics amendment, they create a *Site Governance Amendment Request* form as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the amendment and makes an authorisation decision.

The RGO notifies the PI of amendment authorisation, and this should be shared with the sponsor/CRO (who can also access the authorisation information in ERM, if given appropriate permission).

An amendment must only be implemented **after** it is approved by the reviewing HREC **and** authorised at the institution, and the sponsor/CRO is informed.

Prompt action at each site reduces the gap between ethics approval and SSA authorisation for implementation of an amendment.

4.3.1.2 Request a research governance/SSA amendment

Local changes to site conduct of a research project may require only a research governance amendment, and not need ethics approval. Examples of a site governance issue include: addition of a new Associate Investigator; change of site contact details on a PICF; fees variation; research agreement amendment;

administrative amendment. If unsure, the site PI should discuss a possible amendment with the RGO to determine the type of review required.

For a governance-only amendment, the PI/trial coordinator creates a *Site Governance Amendment Request* form as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the amendment and makes an authorisation decision, then notifies the PI. An amendment must only be implemented **after** it is authorised at the institution.

4.3.2 Safety reports

All safety reporting must align with NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*, in which safety monitoring and reporting to the reviewing HREC is assigned to the sponsor of the research project. Some types of safety event require time-critical reporting to the reviewing HREC, and the CPI or PI may action reporting where appropriate.

The site PI can discuss a safety event with their RGO at any time for advice on reporting. The RGO can also advise on incident reporting in line with the institution's clinical governance reporting requirements (may include an incident report under VHIMS or Riskman, reporting to the reviewing HREC, or notifying legal services and VMIA).

The CPI and/or PI should:

- Capture and assess all adverse events (AEs) that occur at the site as required and in accordance with the protocol
- Report to the sponsor within 24 hours of becoming aware of the event:
  - All serious adverse events (SAEs), except those identified in the protocol as not needing immediate reporting
  - Any occurrences of congenital anomaly/birth defect arising from any pregnancy of a participant (or partner)
  - All urgent safety measure instigated by the site
- Report to the sponsor as specified in the protocol:
  - All safety critical events
  - Any additional requested information relating to reported deaths
- Report to the institution within 72 hours of becoming aware of the event:
  - All significant safety issues
  - SUSARs or USADEs arising from the local site.

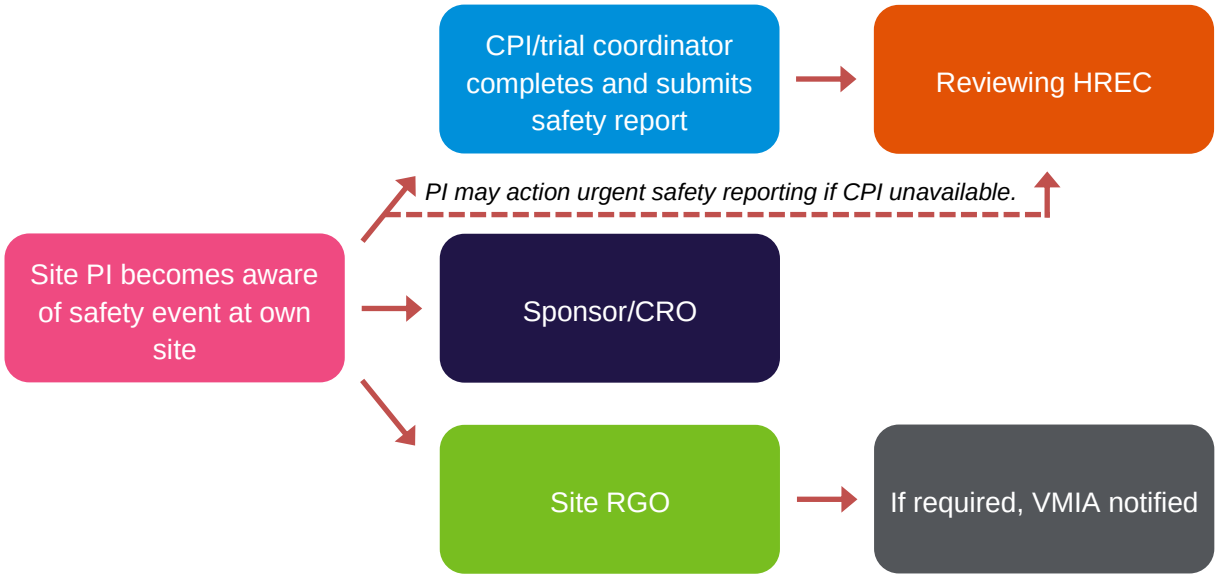
VMIA must be notified of any SUSAR or USADE that occurs at a site in Victoria. They should be informed as soon as possible, concurrent with notifying the HREC. The institution is responsible for reporting to VMIA regarding participants at their site. Email miclaims@vmia.vic.gov.au with:

- A copy of the safety report form completed for the reviewing HREC
- Additional participant specific details such as name, date of birth, trial and/or identification number. The participant's identity is required in the event that an insurance claim arises.

A safety event must be notified to the reviewing HREC. For reporting to a HREC in Victoria, a *Safety Report* is created as a sub-form of the HREA in ERM. Supporting documents are uploaded to the report and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt, and may provide instruction.

The CPI or sponsor/CRO notifies each site PI of the event and the HREC's response, and the PI notifies the site RGO via ERM. The PI/trial coordinator creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt, and may provide instruction.

The site (institution) bears the legal liability for participants. In an instance of a high-risk safety event, the institution could suspend or close the research project at the site. Suspension can later be lifted if the RGO is satisfied the risk has been mitigated.



4.3.2.1 Annual safety report

An annual safety report is required for an interventional clinical trial, in line with NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*. The timing of the annual safety report is at the discretion of the reviewing HREC; they may specify a date or it may align with the sponsor/CRO's reporting cycle. Consult the reviewing HREC's website for information.

For reporting to a HREC in Victoria, an *Annual Safety Report* is created as a sub-form of the HREA in ERM. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt.

The PI notifies the site RGO via ERM. The PI/trial coordinator creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents (including a copy of the *Annual Safety Report*) are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt.

4.3.3 Breach reports

Breach reporting must align with NHMRC's *Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods*.

The site PI can discuss a potential breach with their RGO at any time for advice on reporting.

The CPI and/or PI should:

- Ensure the trial team is aware of the process for reporting serious breaches
- Report any suspected breaches to the sponsor within 72 hours of becoming aware of the suspected breach.

Exceptionally, the investigator, in liaison with their institution, may report the suspected breach directly to the HREC

- Report all serious breaches that have been confirmed by the sponsor as occurring at the site to their institution within 72 hours of being notified of the serious breach
- Provide any follow-up information as required
- Work with the institution or sponsor, as appropriate, to implement any corrective and preventative actions that may be indicated.

A serious breach or suspected breach must be notified to the reviewing HREC. For a Victorian HREC, a *Serious Breach Report* or *Suspected Breach Report* (as applicable) is created as a sub-form of the HREA in ERM. Supporting documents are uploaded to the report and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt.

The CPI or sponsor/CRO notifies each site PI of the breach and the HREC's response, and the PI notifies the site RGO via ERM. The PI/trial coordinator creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt.

A non-serious breach occurring at a site may be notified to the RGO, at their discretion. The site PI should discuss a possible non-serious breach with the RGO to determine if reporting is required. To report a non-serious breach, the PI/trial coordinator creates a *Non-serious Breach/Deviation Report* form as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt.

If a serious breach occurs at the PI's own site, they should discuss it with their RGO. If the RGO wishes to be notified via ERM concurrent with the HREC review, the PI creates a *Site Notification Form* as a sub-form of the SSA, completes it and submits to the RGO. The PI may later provide additional information to the RGO regarding the HREC review.

4.3.4 Progress reports

Information on the progress of an approved research project must be provided to the reviewing HREC in accordance with NHMRC's *National Statement on Ethical Conduct in Human Research*.

The schedule for reporting on a project is determined by the reviewing HREC and RGOs. The frequency of reporting is detailed in the ethics approval letter and research governance/SSA authorisation letter.

The CPI is responsible for reporting to the reviewing HREC for all approved sites. To compile a progress report for a multi-site project, the CPI/trial coordinator (or sponsor/CRO) gathers information from all site PIs/trial coordinators. This should be done well in advance of the report due date. The site PI/trial coordinator should supply their information in a timely manner to allow the CPI to fulfil reporting obligations for the project.

For a HREC in Victoria, the CPI/trial coordinator creates a *Project Progress Report* as a sub-form of the HREA in ERM. Aggregate information for all sites approved by the HREC is included in the report. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for review and acknowledgement.

The site PI is responsible for reporting to the RGO regarding progress at their site, in line with site policy. The PI/trial coordinator creates a *Site Progress Report* as a sub-form of the SSA in ERM. Supporting documents can be uploaded to the report and it is submitted to the RGO. The RGO reviews the report and acknowledges receipt.

4.3.5 Closure

The reviewing HREC must be notified when a research project closes, or when a site closes from an ongoing multi-site project. The RGO must be informed when their own institution's site closes.

If one site closes from a multi-site project that is continuing at other sites approved by a Victorian HREC, the CPI/trial coordinator creates a *Site Closure Report* as a sub-form of the HREA in ERM. When the research project is completed at all sites approved by a Victorian reviewing HREC, the CPI/trial coordinator creates a *Project Final Report* as a sub-form of the HREA in ERM. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for review and acknowledgement. The research office must record the project as '**Closed**' in ERM.

The site PI is responsible for reporting to the RGO regarding site closure or project completion. The PI/trial coordinator creates a *Site Progress Report* as a sub-form of the SSA in ERM. Supporting documents are uploaded and it is submitted to the RGO. The RGO reviews the report and acknowledges receipt. The RGO records the research governance/SSA record '**Closed**' in ERM.

4.3.6 Other post-authorisation reports

A *Site Audit Report*, *Complaint Report* and *Site Notification Form* are available in ERM for reporting to the site RGO. The PI should use these forms as required by their RGO. Each form is created as a sub-form of the SSA in ERM. It is completed, signed and submitted using ERM and then processed by the RGO.

5 Research Governance Officers

5.1 Getting started

5.1.1 Key actions and arrangements

The RGO role can vary among institutions. For clarity on the RGO's responsibilities it is important to have a RGO scope of practice, including formal delegation of authority, from the institution. Sites are strongly advised to articulate the responsibilities with formal delegation within the institution. The RGO's scope of practice could include some or all of the following:

- Management of documents and actions by the RGO in ERM to securely store all documentation relating to the project
- Manage non-standard contracts and standard (pre-agreed) contracts (Medicines Australia and MTAA)
- Communication with internal and external stakeholders (executives, legal department, sponsor/CROs, collaborative groups, investigators)
- Manage assessment of departments that may be impacted by the project and making decisions related to assessment outcomes
- Manage notification to Radiation Safety, Department of Health, for projects involving ionising radiation above dose constraint of ARPANSA code
- Manage final SSA authorisation, including authorising and generating the SSA authorisation letter in ERM
- Make recommendation to executives to not participate in research and not authorise the SSA
- Manage research misconduct.
- Ongoing institutional oversight throughout life of project e.g. managing post-authorisation, conducting audits

The institution's policy on research should be available to both the RGO and investigators in accordance with *The Australian Code for the Responsible Conduct of Research*.

5.1.2 Communication

The RGO may contact the site PI, reviewing HREC office or the sponsor/CRO in order to progress queries. The RGO should retain a clear and accurate record of this communication with an audit trail.

5.1.3 ERM

ERM is used to manage ethics and research governance at public health organisations. There are two aspects to ERM – one for applicants and the other for reviewers (RGOs, HREC coordinators and HREC members). RGOs use the **reviewer** site at https://vic.review.ethicalreviewmanager.com.

Access to the reviewer ERM site is granted after training has been completed. For information on ERM training for RGOs, and the *Research Office User Guide to ERM,* contact multisite.ethics@health.vic.gov.au.

ERM is integral to the RGO role. It is used to manage the SSA form and supporting documents (the core documents for site governance and site assessment) and communications regarding the application.

The site PI/trial coordinator uses the applicant ERM site to complete the SSA form, upload supporting documents, sign and submit to the RGO. They can submit the SSA any time after the ethics application has

been submitted to the reviewing HREC. If the RGO requests SSA information from the site PI, the response must be submitted via ERM in order for the SSA application to proceed.

The SSA form in ERM is linked to the ethics application form (or MDF). Once the SSA has been submitted, the RGO has access to the ethics supporting documents (e.g. protocol) in ERM. In order to maintain document version control, the site PI/trial coordinator should **not** include *ethics* supporting documents in the SSA application.

RGOs should be familiar with the **applicant** ERM site https://au.forms.ethicalreviewmanager.com so they can support researchers at their institution; contact multisite.ethics@health.vic.gov.au to arrange training. RGOs can access both ERM sites using the same login details.

5.2 Research governance/SSA application

5.2.1 Documents

It is recommended that early submission of the SSA and supporting documents to the RGO occurs in parallel with the HREC review process. This allows scrutiny of the study to meet the legal and business requirements of the institution prior to the HREC's decision.

Legal and financial documents are the main items for early attention. Review of these can be time consuming and, in some instances, can delay SSA authorisation.

In ERM, ethics supporting documents are located with the ethics application or project. The RGO must ensure they are viewing only the *approved* version of an ethics supporting document (archived versions are also stored but should not be used for reference). SSA supporting documents are on the 'Documents' tab of the submitted SSA. For guidance, refer to the *Research Office User Guide to ERM.*

5.2.1.1 Document quality check

Recommended practice is to conduct a thorough check of the quality of documents with particular attention to the legal documents. Any unmet requirements should be addressed by the time the HREC decision is made.

The main considerations are:

- Sponsor name (enterprise business name), ABN, address and contact details must be the same on the:
  - Certificate of insurance
  - Indemnity form
  - Standard CTRA or CIRA
  - CTN or CTA.
- Non–standard CTRA (if accepted by the institution) – legal review
- Overall assessment of the proposed research and documents include the:
  - SSA form
  - SSA supporting documents
  - Site-specific documents (optional)
  - Ethics application supporting documents

    These provide the RGO with a complete overview of the research project, so they can assess the suitability of the research and risk to the institution. All documents related to the SSA and ethics application are available in ERM.

The RGO should assess the document quality associated with the SSA application. In ERM they should record that the whole application has been received, or it is a partial application and request information from the PI/trial coordinator. The request to the PI/trial coordinator should be as specific as possible, to enable them to provide a timely response. The PI/trial coordinator must submit a response via ERM so the application can proceed.

5.2.2 Key documents for RGO's assessment

Document	Description	RGO Process
Protocol	Ethics supporting document containing research project details	• Ensure viewing the *approved* ethics supporting document in ERM. • Assess impact on institution's resources.
Investigator brochure or Instructions for Use	Ethics supporting document containing clinical trial background information including mechanism of action and use in humans (IB) or infection prevention and safety compliance (IFU).	• Ensure viewing the *approved* ethics supporting document in ERM.
VSM	Ethics supporting document addressing Victorian legislative requirements.	• Ensure viewing the *approved* ethics supporting document in ERM. • Assess appropriateness of research at site.
Copy of ethics approval letter	A letter/certificate issued by a Victorian reviewing HREC or NMA-accredited reviewing HREC to confirm their ethical review and approval of the research proposal. Includes list of approved documents, sites and any approval conditions.	• Check letter/certificate is issued by a Victorian reviewing HREC or NMA-accredited reviewing HREC. • Check letter/certificate includes: – approval date – correct project details – list of approved sites. • Check that all documents listed on the letter are in ERM for review.
Research agreement (CTRA or CIRA or other)	Legal document between institution and sponsor/CRO which agrees terms of conducting the project at the site; usually contains site budget. Research that involves multiple parties requires an agreement, unless written authorisation to waive this requirement is	• Information is in Section 5.2.2.1 • Review of research agreement can be protracted; begin as early as possible, perhaps when document is in draft form. • Finalise signature of CEO or delegate.

Document	Description	RGO Process
	obtained from the responsible executive.	
PICF with site-specific details	The reviewing HREC approves the master template of the Participant information and consent form (PICF), and site specific details may be added by the site research team. The main body of the approved master PICF must not be altered, only practical site details (e.g. contact information) may be added.	• Check: – site-specific PICF matches Master PICF – track-changed and clean versions of PICF showing changes in the Master with site version details – footer refers to both the Master and the local governance versions – Site Master PICF includes any HREC-approved special site clauses • A site may only amend the Master PICF site contact details (researcher and complaints) and the site letterhead. • Site contact details required: – site PI name and position – site contact details (including emergency contact) – 24-hour contact details – contact details for complaints.
Standard Form of Indemnity	Indemnity covers the potential liability of each party involved and the insurance requirements.	• The Medicines Australia or MTAA Standard Form of Indemnity must be used if the study is commercially sponsored. • Appendix 7 can be used to assist with review. • Ensure the form of indemnity is populated with the correct information. Legal entity details must be the same as in the CTRA/CIRA and CTN. • Each site must have a separate indemnity form for conduct of the trial at the institution. • Verify form(s) have been signed by the sponsor. • Finalise signature of CEO or delegate.
Insurance Certificate	A commercial sponsor must provide evidence that it has appropriate and adequate insurance for the study in the form of a certificate of currency.	• Ensure cover for the risk of conducting a trial. Legal entity details must be correct – check name and spelling.
Evidence of CTN or CTA	Notification or approval from TGA for unapproved therapeutic	• Information is in Section 3.4. • CTN: Check submission to the TGA.

Document	Description	RGO Process
	goods to be supplied for experimental purposes in humans.	• CTA: Check approval issued by the TGA. • Check site information is correct. Legal entity details must be the same as in the CTRA/CIRA and indemnity form. • For investigator-initiated research, RGO may facilitate the CTN submission with investigators.
Detailed site budget	Usually part of the research agreement. Budget must demonstrate that institutional costings have been adequately accounted for and agreed, and can be tracked.	• RGO should advise the research team if a draft is acceptable at an early stage – budget agreement can be a lengthy process and negotiation should occur early. • Check the following budget information is included: – CTRA Schedule 2 – 'Payments' – SSA Form – 'Budget' section • Check research governance fees are included.
Investigator CV	Each investigator's CV must indicate their capacity to undertake their role in the project, including specific training (e.g. GCP) required for the research	• Review of CV should clarify whether an investigator has the skills to undertake the research. Ensure the CV is current – an abbreviated version is acceptable. If RGO determines CV is inadequate, discuss concerns with the research team.
Evidence of professional registration	Certificate or evidence from professional or peak body.	• Ensure each investigator is appropriately registered.
Evidence of GCP training	If relevant to the type of clinical trial, each investigator must provide proof of recent Good Clinical Practice (GCP) training.	• Evidence of GCP training/certification should be reviewed for currency. • Evidence should be provided for all investigators at the site. • Information on training providers is at www.transcelerate-gcp-mutual-recognition.com/view-course.
Drug committee approval	If relevant to the type of clinical trial and practice of the reviewing HREC, the research proposal may be reviewed by a drug committee.	• Check approval information. • Assess appropriateness of research at site.
Biosafety approval	If relevant to the type of clinical trial and practice of the site, research may be reviewed by an institutional biosafety committee.	• Check approval information. • Assess appropriateness of research at site.

Document	Description	RGO Process
Radiation safety approval	Supporting documents for a project involving ionising radiation. Information is in Section 3.7 and Appendix 4.	• Information is in Section 5.2.2.2. • Ensure viewing the *approved* ethics supporting document in ERM.
Embryo research licence	Research on human embryos can only be conducted under a licence issued by the NHMRC Embryo Research Licensing Committee.	• Check information in the embryo research licence. • Assess appropriateness of research at site.
Approval of genetically modified organisms	Use and release of genetically modified organisms is regulated. Approval processes differ for GMO types. See www.ogtr.gov.au/apply-gmo-approval/types-gmo-dealings#clinical-trials. An institutional biosafety committee (IBC) must endorse all gene-related therapy assessments, The IBC may assist with preparation of an application to the OGTR for a Dealing Not Involving Intentional Release (DNIR) licence or a Dealing Involving Intentional Release (DIR) licence.	• Check IBC approval information. • Verify licence information (or exemption, if applicable). • Assess appropriateness of research at site.
Research governance review fee	Payment for research governance review.	• RGO's institution's practice/policy

5.2.2.1 Research agreement

For general information on research agreements, see Section 3.5.

Review of the research agreement can be lengthy and may slow the SSA review process. The RGO should encourage the PI to submit the SSA with research agreement as early as possible, in parallel with the ethics review process. This allows the RGO time to begin an early review of the research agreement. The RGO may accept a draft version of the research agreement and its budget information for initial review.

- Medicines Australia (MA) information and CTRA templates are at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/

- Medical Technology Association of Australia (MTAA) information and CIRA templates are at www.mtaa.org.au/clinical-investigation-research-agreements
- Investigator initiated CTRA is at www.clinicaltrialsandresearch.vic.gov.au/research-governance-applications
- CTRA Teletrial subcontract between primary site and satellite site is at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements

CTRA and CIRA Schedules 4 and 7 that have been agreed by the SEBS panel are posted on a secure portal for Victorian RGOs. The portal is hosted by the Coordinating Office for Clinical Trial Research and is available to RGOs at all sites participating in the Victorian framework to streamline clinical trials. For access to the portal, email multisite.ethics@health.vic.gov.au.

The RGO should verify the CTRA or CIRA against the standard template, and verify submitted Schedules 4 and 7 against the SEBS-agreed clauses. If the Schedule 4 or 7 does not match the SEBS-agreed version, contact multisite.ethics@health.vic.gov.au.

Appendix 6 can be used to assist with review of a research agreement. Tips for review of a research agreement:

- Understand the project
- Be consistent and clear in requests for changes
- Understand the institution's position on investigator-initiated or collaborative group research in terms of funding expectations
- Understand the key points in the research agreement to check and use the SEBS approval.

Common issues that arise:

- Inaccurate sponsor name due to use of agency relationships
- Special conditions incorrectly inserted into Schedule 2 (they must **only** be in either Schedule 4 or 7, as applicable to the template)
- Sub-contracting to third party payers
- Size and volume of budget
- Additional special conditions to pre-agreed templates

Institutions are encouraged to use electronic signature where possible. The document should be reviewed by both parties prior to any signature being applied. Both parties must also agree to the use of electronic signatures.

For a teletrial, a CTRA subcontract agreement between the primary site and satellite site is required for each satellite site. This is in addition to the CTRA (head agreement) between the sponsor and primary site.

For an institution that accepts non-standard agreements, the recommended practice is that local legal review is sought for any non-standard agreement. The RGO must notify the sponsor/CRO before the legal review is conducted; the commercial sponsor is responsible to pay for legal review.

5.2.2.2 Radiation safety approval

For general information on research involving ionising radiation, see Section 3.7.

The RGO should be familiar with the *Radiation Protection Series No. 8 Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes* and the ARPANSA Radiation Health Committee's Statement on ethical review for multi-centre trials. Additional information is in Appendix 4.

If the site's radiation exposure is part of standard clinical care, the ethics supporting documents should include a site PI letter to confirm. The RGO should check the information in the letter.

If the site's radiation exposure is additional to standard clinical care, the RGO must receive an assessment report by a Medical Physicist. The RGO must review the Medical Physicist report and also check other documents for adherence to the report (e.g. verify corresponding information is in site PICF).

If the protocol's ionising radiation level is additional to standard of care at the site, the RGO should consider:

- Review of their site's radiation safety risk assessment (either the Notification to reviewing HREC form or the Medical Physicist's report) and the ethics approval letter.
- The Medical Physicist's report should clearly state the Risk Category as defined in the *Radiation Protection Series No. 8 Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes*.
- The ethics approval letter should list the radiation risk category considered by the reviewing HREC in giving its approval.
- If the radiation risk category assessed by the site is the same as or lower than the risk category on the ethics approval letter, the radiation risk can be accepted as part of the research governance/SSA authorisation without the need for further HREC review.
- If the radiation risk category assessed by the site is deemed higher than that on the ethics approval letter, an ethics amendment would be required – the site PI should contact the CPI regarding submitting an ethics amendment application.

If dose of radiation is **above** dose constraint of ARPANSA Code, the RGO must ensure the Radiation Team at DH is notified (can be after authorisation). The RGO may action the DH notification, or verify that it has been done by another party.

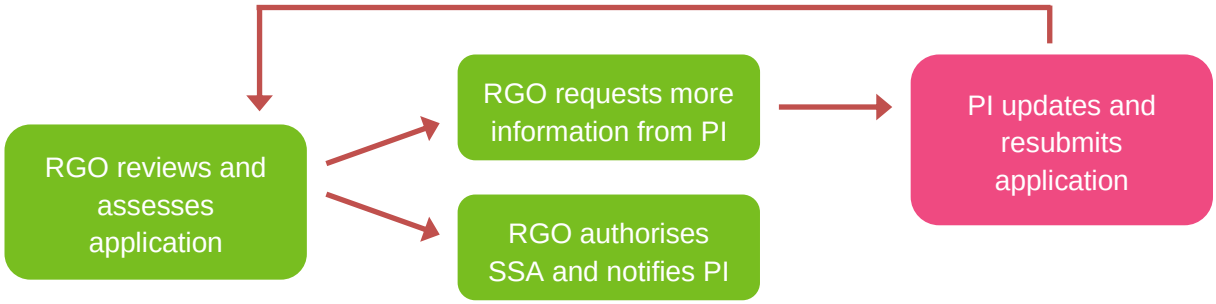
5.2.3 SSA review

Following early submission of the SSA (before ethics approval) and checking by the RGO, the RGO should record the application as 'partial application' in ERM to allow the PI/trial coordinator to resubmit the SSA with the ethics approval letter.

The RGO has access to the ethics supporting documents (e.g. protocol) in ERM after the SSA form has been submitted. In order to maintain document version control, the site PI/trial coordinator should **not** include *ethics* supporting documents in the SSA application.

The RGO must refer to the *approved* ethics documents (located on the ERM ethics application or project) as well as the SSA supporting documents on the SSA's Documents tab in ERM. For guidance refer to the *Research Office User Guide to ERM*. If the RGO requires more information, they use ERM to request it from the PI/trial coordinator, who submits the response via ERM. The request to the PI/trial coordinator should be as specific as possible, to enable the PI/trial coordinator to provide a timely response.

Process for SSA review



5.2.4 SSA authorisation

Once the RGO is satisfied that the submission is complete, the recommendation can be made to the CEO or delegate, who has the authority to authorise the research at the site. On the basis of the RGO's recommendation the CEO or delegate decides whether the project is authorised or not authorised.

The authority delegated to the RGO varies among institutions. In one model, the RGO assesses the submission and makes a recommendation to the CEO or delegate for final authorisation. If the RGO has delegated authority, the recommendation step is unnecessary and they can make the decision themselves.

The outcome must be recorded in ERM and the appropriate letter sent to the site PI.

A complete record of documents must be kept by the RGO, including the fully executed CTRA and indemnity forms. It is recommended that the RGO uses ERM to securely store all documentation electronically for the project.

5.2.5 SSA notification to PI/trial coordinator

The PI should be notified of the SSA authorisation decision within one working day of the decision date. For efficiency, it is recommended to send an ERM-generated letter as it is auto-populated with application information and document details.

5.3 During the research project

The site RGO is responsible for monitoring the conduct of the research project at the site. Accordingly, the site PI has ongoing responsibilities to report to the RGO throughout the duration of the research project.

Information on monitoring and reporting is at www.clinicaltrialsandresearch.vic.gov.au/monitoring-and-reporting.

Reporting should align with the National Health and Medical Research Council (NHMRC) guidance *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*.

In Victoria, post-authorisation reporting is managed in ERM. For information, see Appendix 2 and refer to the *Research Office User Guide to ERM*.

5.3.1 Amendments

An amendment is a written change to an HREC-approved protocol for ongoing research. Irrespective of HREC approval, an amendment may have a minor or a substantial impact on research governance/SSA at the site.

Unless there is an urgent safety issue, an HREC approved amendment cannot be implemented at a site until the RGO has assessed and authorised the amendment. While the RGO manages the authorisation process, the delegated authority for authorisation may vary depending on the impact of the amendment on the institution.

Changes that may impact on the institution should be assessed carefully and may require sign-off from departments involved. Major amendments could involve:

- Type of study medications
- Number or type of tests required
- Number of participants
- Research project end date
- Extension to the research project.

Type	Description	Example	RGO Action
Minor Amendment	Change to the details of research that has no significant implications for participants or for the conduct, management or scientific value of the study. • Correction of typographical errors in the protocol or other study documentation • Amended contact details for sponsor or project staff	Administrative update, minor safety update, budget update, change of CPI or site PI, change in number of participants, change of end date, minor contractual changes.	Review information and ethics approval. If required, seek advice from PI and/or CEO/delegate. Authorise SSA amendment at the site and action the amendment.
Major Amendment	Amendment to protocol or any other supporting documentation that is likely to affect, to a significant degree: • Safety/physical/mental integrity of participants • Scientific value of trial • Conduct/management of trial • Quality or safety of investigational product	Significant change/impact on department(s), contractual change, change to investigational drug or device, change to number of study procedures, restarting project after a safety issue.	Make recommendation to CEO/delegate about SSA authorisation. CEO/delegate may request further advice from legal or other avenues. CEO/delegate decides how to progress and RGO takes action.

Type	Description	Example	RGO Action
Site governance-only amendment	• Site-specific administrative change with no ethical impact.	Addition of site associate investigator.	Review information and authorise SSA amendment at the site.

The CPI notifies the reviewing HREC of a proposed amendment (in Victoria, this is done via an *Ethics Amendment Request*). Following HREC approval of an amendment, the CPI notifies the PI. In ERM, the PI submits a *Site Governance Amendment Request* to the RGO. The supporting documents provided by the PI should include a copy of the amendment's HREC approval as well as copies of changed documents and any site-specific documents, including tracked-changes copies.

A site governance-only amendment that does not impact ethics approval (e.g. addition of new associate investigator) can be notified to the RGO only; the reviewing HREC does not need to be informed. In ERM, the PI completes a *Site Governance Amendment Request,* uploads supporting documents and submits to the RGO.

For all SSA amendments, the RGO reviews the information submitted by the PI and processes the SSA amendment in ERM. The RGO can request further information from the PI if required; the PI must resubmit via ERM.

To allow an amendment to be implemented at the site as quickly as possible, the RGO should notify the PI of authorisation promptly. Using an ERM-generated authorisation letter is a fast and efficient way to communicate the outcome.

The timeline for processing an amendment is important, as a research project may be temporarily suspended and medical treatment of participants could be disrupted. Delay in SSA authorisation of an amendment may result in an impact on participant recruitment, treatment, project costs and data management.

The RGO must notify the PI/trial coordinator of authorisation of a SSA amendment within one working day of the decision.

5.3.1.1 Amendment involving ionising radiation

An amendment to the protocol may involve a change in frequency, number or modality of ionising radiation procedures. If the radiation level is additional to standard care, a revised Medical Physicist's report is required for the site.

The CPI must submit an ethics amendment request to the reviewing HREC. If a protocol amendment results in an increase in the radiation dose which moves it to a higher radiation risk category (in accordance with *Radiation Protection Series No. 8 Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes*), the CPI must submit Medical Physicist report(s) with the amendment request. The CPI must refer to the reviewing HREC's policy: either all sites' Medical Physicist reports will be required, or the report from the site with the highest assessed dose.

The revised radiation risk category should be listed on the ethics amendment approval letter. When the RGO is informed of the ethics amendment, they must assess their site's radiation safety risk assessment. The site's risk category must be the same as or lower than the risk category listed on the ethics amendment approval letter (if higher, a further ethics amendment would be required).

5.3.2 Safety reports

All safety reporting must align with the NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* in which safety monitoring and reporting to the reviewing HREC is assigned to the sponsor of the research project.

The RGO should:

- Assess whether any received safety report impacts participant safety, data integrity on medico-legal risk, the responsible conduct of research, adherence to contractual obligations or the trial's continued site authorisation and, where applicable, facilitate the implementation of corrective and preventative action
- Ensure site investigators have clear guidance detailing the requirements for safety reporting and monitoring in clinical trials. The guidance should cover the requirements for both externally sponsored clinical trials and, if applicable, internally sponsored investigator/initiated or collaborative group trials.

Investigators (and, if appropriate, the sponsor/CRO) are encouraged to discuss any safety events with the RGO for guidance on reporting and responsibilities.

A safety event is reported to the reviewing HREC (in Victoria, a *Safety Report* is used) and the CPI notifies the PI of the outcome. In ERM, the PI submits a *Site Notification Form* with supporting documents (including a copy of the *Safety Report* and any subsequent HREC correspondence) to the RGO. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

If a high-risk safety event occurs during a research project, the institution can suspend or close the research project at the site. The site (institution) bears the legal liability for the participants. Suspension or closure must be recorded in ERM and urgently communicated to the PI. Suspension can later be lifted if the RGO is satisfied the risk has been mitigated.

The site RGO should ensure the research team action incident reporting in line with the institution's clinical governance reporting requirements. This may include an incident report under Victorian Health Incident Management System (VHIMS) or Riskman, reporting to the reviewing HREC, or notifying legal services and VMIA.

5.3.2.1 Annual safety report

For an interventional clinical trial, an annual safety report is submitted to the reviewing HREC, in line with NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*. Following review by the HREC, the site PI should notify the RGO with a copy of the annual safety report.

In ERM, the PI submits a *Site Notification Form* with supporting documents (including a copy of the *Annual Safety Report* and any subsequent HREC correspondence) to the RGO. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

The RGO should consider the *Annual Safety Report*'s relevance at their site and ensure any local site safety monitoring and reporting guidelines have been followed.

5.3.3 Breach reports

Breach reporting must align with NHMRC's *Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods*.

Investigators (and, if appropriate, the sponsor/CRO) are encouraged to discuss any breaches with the RGO for guidance on reporting and responsibilities.

The RGO should:

- Develop clear guidance for investigators detailing the reporting and management of serious breaches
- Take advice from the reviewing HREC regarding its assessment of the breach
- Assess each serious breach to determine its impact, e.g. any impact on other trials conducted by the institution/investigator
- Facilitate the implementation of any corrective and preventive actions if required by the sponsor or institution
- Inform the HREC if a serious breach leads to withdrawal of the site's authorisation, if the research team has not already informed the HREC
- Consider whether the conduct determined to be a serious breach requires the application of the *Australian Code for the Responsible Conduct of Research*.

A breach is reported to the reviewing HREC (in Victoria, a *Serious Breach Report* or *Suspected Breach Report* is used) and the CPI notifies the PI of the outcome. In ERM, the PI submits a *Site Notification Form* with supporting documents (including a copy of the report and any subsequent HREC correspondence) to the RGO. The RGO assesses it and processes in ERM, then acknowledges it to the PI.

If the breach occurs at the PI's site, they may submit a *Site Notification Form* to the RGO in parallel with the HREC review. This allows the site RGO to assess any potential risk as early as possible.

The institution can suspend or close the research project at the site. The site (institution) bears the legal liability for the participants. Suspension or closure must be recorded in ERM and urgently communicated to the PI. Suspension can later be lifted if the RGO is satisfied the risk has been mitigated.

It is at the RGO's or institution's discretion whether to be notified of a non-serious breach. The site PI should discuss a possible non-serious breach with the RGO or refer to site guidelines to determine if reporting is required. To report a non-serious breach, in ERM the PI/trial coordinator completes a *Non-serious Breach/Deviation Report* form, uploads supporting documents and submits it to the RGO. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

5.3.4 Progress reports

Project progress reports are required at least annually by the reviewing HREC for ongoing ethics approval, and site reporting to the RGO is also required. The schedule for reporting on a project is determined by the reviewing HREC and RGOs. The frequency and timing of reporting must be detailed in the ethics approval letter and research governance/SSA authorisation letter.

The CPI is responsible for reporting to the reviewing HREC for all approved sites. In Victoria, the CPI aggregates information for all sites approved by the HREC, and a *Project Progress Report* is submitted to the HREC for review and acknowledgment. If the reviewing HREC does not receive the progress report in a timely manner, the research project may be suspended at a site until a report is provided.

The PI can notify the RGO of overall project progress via a *Site Notification Form*, and include a copy of the *Project Progress Report* as a supporting document. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

The site PI is responsible for reporting to the RGO regarding progress at their own site, in line with site policy. In ERM the PI/trial coordinator submits a *Site Progress Report* to the RGO. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

When reviewing a *Site Progress Report*, the RGO should pay particular attention to the project's current status, recruitment in relation to targets, site audit and budget information, and certificate of insurance. If any

information seems unusual or requires more explanation, the RGO requests more information via ERM and the PI resubmits with the requested information.

5.3.5 Closure

A particular site may close or the entire research project may be completed; the CPI is responsible for notifying the reviewing HREC. The RGO must be informed when their site or the project closes.

The CPI/trial coordinator notifies the reviewing HREC of site or project closure. In Victoria, this is done using a *Site Closure Report* (if one site closing) or a *Project Final Report* (if project completed). In ERM, the PI submits a *Site Notification Form* with supporting documents (copy of the report and any subsequent HREC correspondence) to the RGO. The RGO reviews it and processes in ERM, then acknowledges it to the PI.

The research project close-out process ensures the file is complete. The RGO must confirm all required documents and reports are received and acknowledged and the final report has been processed appropriately. The RGO must record the research governance/SSA record as '**Closed**' in ERM.

Clinical trial records are retained for a minimum of 15 years or may be longer for paediatric trials. The RGO should check with their institution regarding site policies on file retention, archiving and destruction.

5.3.6 Other post-authorisation reports

The RGO should consider how they wish to utilise the *Site Audit Report*, *Complaint Report* and *Site Notification Form* that are available in ERM for the PI to complete. The RGO should communicate to PIs regarding when these forms should be used.

Researchers should be encouraged to complete a *Site Audit Report* at a scheduled time advised by the RGO (e.g. three months after SSA authorisation).

A misconduct policy should be in place at the institution, and be adhered to in the event of receiving a *Complaint Report*.

When a PI submits a *Site Audit Report*, *Complaint Report* or *Site Notification Form*, the RGO reviews and processes it in ERM.

5.3.7 Research audits

To oversee research conducted at the institution, the RGO may perform research audits. The purpose of a research auditing program is to review how research is conducted and to detect, correct and prevent potential and existing shortcomings. In addition to regular progress reports from the researcher, audits may include:

- Full audit or site visit by the research governance office
- Desktop audit or self-audit (using the *Site Audit Report* in ERM)
- Themed/targeted audits.

6 Industry sponsor and Contract Research Organisation

Terminology: Throughout this document, sponsor and Contract Research Organisation (CRO) are referred to together. ‘Sponsor/CRO’ encompasses related personnel.

6.1 Getting started

6.1.1 Site selection

Early action from the sponsor/CRO is crucial in successfully gaining ethics, research governance and regulatory approval in an efficient and timely manner. The sponsor/CRO should obtain all available supporting project documentation from the local or global project team as early as possible. Ideally, these documents should be provided to sites at the time of site selection and feasibility.

Supporting documents include but are not limited to:

- Protocol
- Investigator brochure
- Master PICF
- Relevant background information.

During site selection the following should be considered:

- Discuss with each site PI the requirements of their site RGO
- Conduct an evaluation to determine which will be the CPI (lead) site and participating sites
- Make draft budgets known to sites. This includes details of allowances for the CPI coordinating the trial. Address negotiations about budget and any other issues
- Establish a clear communication plan to determine the flow of correspondence between the CPI and participating sites, and whether the sponsor/CRO has partial responsibility for document flow
- Understand each site’s RGO authorisation process
- Ensure staff training requirements are met and staff have appropriate experience with clinical trial research
- Timeliness for the process and the sponsor/CRO’s expectations for submission to the RGO should be clear to all parties
- Ensure the research team have access to ERM and are familiar with its use, or undertake training (see www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager)
- Establish a plan for ownership of each site’s SSA form in ERM, and delegation of responsibilities.

A commitment should be sought from the site staff and RGO to conduct research governance in parallel with the ethics review process.

A useful document for reference is the Research Governance Checklist. Download at www.clinicaltrialsandresearch.vic.gov.au/research-governance-applications.

Once sites are selected the sponsor should clarify the communication pathway for trial documents both for ethics and research governance/SSA, including the CPI providing a response to the HREC and ensuring the sponsor/CRO has ERM permission to view that response.

6.1.2 Documents and site contacts

Following confirmation of site involvement, the sponsor/CRO should obtain appropriate details from each site, so all documents submitted to the RGO are consistent. Examples of documents requiring correct entity details:

- the institution's business name and ABN. The ABN lookup at www.abr.business.gov.au is the public view of the Australian Business Register
- a contact for legal notices
- finance contact details
- CTN or CTA
- CTRA or CIRA
- insurance certificate of currency
- indemnity forms (standard and HREC review only).

Where a sponsor has a CRO performing the budgetary negotiations the sponsor should ensure appropriate support and oversight is provided for the CRO. The sponsor's research departments should work to ensure consistency and fairness across contracts.

The site budget is generally reviewed by multiple parties, including the institution's departmental representatives. This detailed review can cause delay in research governance/SSA submission and authorisation. The sponsor/CRO should provide the site budget and draft CTRA or CIRA to the PI at the earliest possible opportunity. This allows the PI to submit early to the RGO so that all parties can commence their review.

The research project site budget procedure costs should be aligned with local procedural costs with consideration of the principles of fair market value. The proposed study budget should not simply be costs converted from a global schedule. The local budget and fees must be fair and reasonable according to acceptable local expectations.

6.1.2.1 Research agreement

For general information on research agreements, see Section 3.5.

- Medicines Australia (MA) information and CTRA templates are at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/
- Medical Technology Association of Australia (MTAA) information and CIRA templates are at www.mtaa.org.au/clinical-investigation-research-agreements
- CTRA Teletrial subcontract between primary site and satellite site is at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements

The sponsor/CRO should use the standard CTRA (medicines) or CIRA (devices) to eliminate the need for legal review at each site and to minimise legal costs.

The RGO's review of the research agreement on behalf of the institution can be lengthy and may slow the SSA review process. It is recommended that the sponsor/CRO prepares the research agreement as early as possible to allow the RGO time for review.

If the sponsor/CRO makes a submission to SEBS for inclusion of 'Special conditions' in Schedule 4 or 7 of the CTRA or CIRA, they should plan ahead for scheduling the review as the SEBS panel meets monthly. Once

agreed by SEBS, the sponsor/CRO receives a notification from each individual SEBS jurisdictional member with a copy of the standard schedule.

To save time and cost in the site assessment process, it is important for the sponsor/CRO to familiarise industry staff with the guidance on seeking special conditions for CTRA/CIRA standard schedules. Guidance on submitting a request to SEBS, including the *SEBS Review Template*, is at www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/ (medicines) and www.mtaa.org.au/clinical-investigation-research-agreements (medical devices).

The sponsor/CRO should provide the research agreement (or a draft) to the PI to be included in early submission of the SSA, in parallel with the ethics review process. The RGO can begin their review early and request information and/or modifications via the PI. Performing this review while the HREC review is underway allows for faster SSA authorisation following ethics approval.

6.1.3 Clinical trials notification (CTN) and Clinical trials approval (CTA)

For general information on CTN and CTA see Section 3.4. Full information is at www.tga.gov.au/clinical-trials.

The Australian clinical trial sponsor must notify the TGA of the intent to sponsor a clinical trial involving an 'unapproved' therapeutic good; this must take place before starting to use the goods.

The sponsor/CRO completes the CTN via the TGA online portal. Prior to using the portal for the first time, the sponsor/CRO must register for a Client ID (information is at www.tga.gov.au/tga-business-services-getting-started-tga). The CTN is completed and submitted online and a fee paid by the sponsor/CRO.

The sponsor/CRO should prepare the CTN early in the start-up process and it should not be rate limiting. All parties should agree on the timing of submitting the CTN. The TGA aims to process a CTN in 5-7 working days, and its status can be tracked via the online portal.

The TGA may give the sponsor/CRO written notice to provide specified information relating to goods notified in the CTN form. A response must be provided in a timely manner to avoid causing any delay.

The sponsor should view the CTN acknowledgement information in the TGA online portal, it can be printed/exported and used as evidence that the clinical trial has been notified to the TGA. The acknowledgement should be provided to the site PI for inclusion in their SSA submission.

When the clinical trial has been completed at all approved sites, the sponsor/CRO must notify the TGA of trial completion. The CTN is used to submit completion advice to the TGA.

A CTA application to the TGA is paper-based and consequently slower than a CTN. It is recommended to consult the TGA early regarding a potential CTA application, and to factor its timing into the ethics and research governance submission timeframe. The approval from TGA should be provided to the site PI for inclusion in their SSA submission.

6.1.4 Indemnity and insurance

Medicines Australia (MA) represents the discovery-driven pharmaceutical industry in Australia and has negotiated industry-accepted standard forms of indemnity. These are considered mandatory formats in Australia and there are two forms of indemnity from Medicines Australia in use:

- The standard form of indemnity is for institutions and staff conducting the clinical trial and HREC review
- The HREC review only form of indemnity is for an HREC that is providing ethical and scientific review for a clinical trial only. In accordance with Medicines Australia: “For use where the Indemnified Party is providing ethical review for a multicentre clinical Study where the ethical review will be adopted by hospitals,

institutions or sites that are independent from the Indemnified Party, OR as a Reviewing HREC for a single centre study at a hospital or institution that is independent from the Indemnified Party."

The MA indemnity forms are at www.medicinesaustralia.com.au/policy/clinical-trials/indemnity-compensation-guidelines.

The Medical Technology Association of Australia (MTAA) represents medical technology companies and has developed forms of indemnity for device clinical trials:

- MTAA Standard Indemnity Form for a clinical investigation
- MTAA Indemnity Form for HREC review only
- MTAA Compensation Guidelines.

The MTAA indemnity forms are at www.mtaa.org.au/clinical-investigation-research-agreements.

Appendix 7 can be used to assist with completion and review of an indemnity form.

Ensure names, legal details, and the correct version number and date are the same on all relevant documents. Documentation must be accurate and correct before it is submitted to the RGO. Otherwise, delays can result.

In Victoria, statewide insurance is provided through VMIA. Details of requirements for clinical trials are at www.vmia.vic.gov.au/~/media/internet/content-documents/risk/guides-and-publications/clinical-trials/clinical-trials-guide.pdf.

Clinical trials must have a certificate of currency for public and products liability insurance from the commercial sponsor.

The certificate of currency must:

- Specifically name the Australian corporate entity acting as commercial sponsor, or if using the global entity name, then the global entity must provide a letter to say the local entity is wholly owned and a named insured under the relevant insurance policy
- Cover the conduct of the relevant clinical trial in Australia
- Be current throughout the entire period in which the clinical trial is conducted
- Not have a defined statute of limitations
- Have acceptable deductibles and level of indemnity
- Have a limit of liability per claim and in the annual aggregate of AUD$20 million for New South Wales and AUD$10 million for other jurisdictions in Australia
- Ensure the excess deductible is no greater than AUD$25,000 for each and every claim or series of claims arising out of one originating cause.

In the event that it is not possible to obtain a certificate of currency that specifically names an insured that is an Australian corporate entity acting as commercial sponsor, it will be sufficient to sight a certificate naming the Australian entity's overseas parent company and its subsidiaries worldwide. This applies if a parent company provides written confirmation of the Australian corporate entity acting as commercial sponsor and is a wholly owned, operated or controlled subsidiary company of the parent, and that such a subsidiary is also a named insured under the relevant insurance policy for the purpose of the conduct of the trial in Australia.

In some Australian jurisdictions global sponsors might be asked to produce insurance to cover any risks which may arise with trial monitors entering a public hospital.

6.1.5 Use of ionising radiation

If the research project involves exposing participants to ionising radiation, specific supporting documents must be included in the ethics and research governance/SSA applications, and there are regulatory requirements. Refer to Section 3.7, and information is at www.clinicaltrialsandresearch.vic.gov.au/ethics-application.

At site selection, the sponsor/CRO must survey participating sites to determine whether the protocol's ionising radiation level is **standard of care** or **additional to standard of care** at each site. If a new site is later added via amendment, the sponsor should also survey that site. The ethics and research governance/SSA processes depend on whether participants will receive a level of ionising radiation that is **part of** standard clinical care, or a level that is **additional to** standard clinical care.

The sponsor/CRO should consult each participating institution's website for guidance on any specific site processes for research involving ionising radiation. This should be done in advance of submitting the ethics and research governance/SSA applications, so all requirements can be met in a timely manner. Site processes must be adhered to, and may incur a fee.

When reviewing the research governance/SSA application, the RGO ensures that all radiation information included in the SSA and ethics application is appropriate for their site, and any local requirements have been met.

6.1.6 Equipment for device research projects

- All unapproved devices need to be listed on the CTN whether they are owned by the sponsor or the device is under investigation.
- Where devices are approved for use in Australia or internationally, an Instruction for Use (IFU) document could be submitted as a replacement for the investigator brochure.
- Studies in which equipment is loaned or stored within a hospital for use for the duration of the study per protocol may require completion of a loan of equipment application form. The equipment may also require to be assessed by Biomedical Engineering for quality assurance prior to installation at the hospital.
- Where pharmaceutical studies adhere to ICH GCP, device trials may be conducted in accordance with ISO-14155.
- During the site initiation visit, training and information is provided regarding protocols, devices and GCP. The site visit should also establish that investigators have sufficient experience with the device or implant and are confident with their use.
- Ensure sufficient time for shipment of unapproved devices, as customs can take some time for processing the documentation and releasing the material.
- All unapproved devices must be labelled appropriately, with wording like "Investigational Use Only".
- The site must have appropriate storage conditions for investigational devices.
- Funding for the device (if applicable) needs to be agreed by all parties during the study set-up.

6.1.7 Communication plan

A clear communication and documentation plan is critical for efficient management of research governance/SSA requirements and for the ongoing conduct of the research project. It should include information on timelines and personnel responsible for the documentation. It should also detail the ERM permissions of research team members to access the ethics application, SSA, post-approval and post-authorisation forms.

The sponsor/CRO should establish a local liaison, ideally the monitor, to communicate with the CPI/trial coordinator and the participating sites. It is imperative that every project has one nominated site and sponsor/CRO contact person who ensures all trial content is maintained, communicated and tracked. It would be most appropriate to assign a trial monitor and a trial coordinator from the coordinating site as the main contact persons.

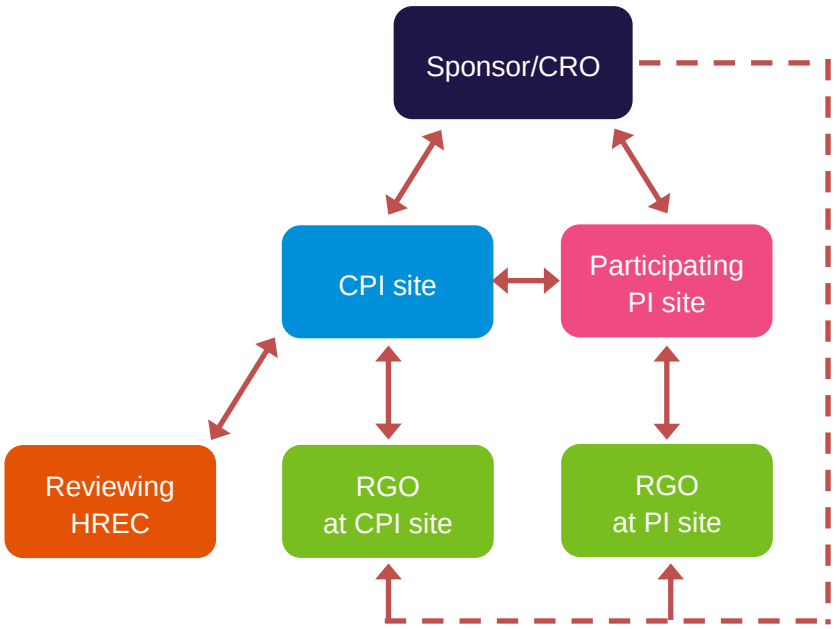
A clear communication strategy, document flow and communication plan should be put in place once the CPI, monitor and participating site PI/trial coordinator are alerted of participation in the research project. The plan should assign responsibilities for:

- HREC submission, study contacts and distribution lists
- Safety and breach reports
- Annual and final reports.

There must be backup arrangements in place so that all research governance/SSA actions can be carried out in a timely manner. These arrangements should be discussed at the initial site meeting and documented in the communication plan and site documents.

The monitor working with the CPI (lead site) is responsible for discussing the communication plan with that site. The CPI's site should communicate the plan to participating sites.

Communication plan – pre-HREC approval



6.2 Research governance/SSA application

6.2.1 Communication

It is imperative that the sponsor/CRO receives all communications from the RGO to ensure participating sites and the CPI are notified. Clear communication is particularly important if prompt follow-up is required from participating sites (e.g. a request for further information or HREC approval notification to the CPI).

The sponsor/CRO should have an appropriate ERM role assigned to them, this allows them to view ethics and research governance/SSA application progress and communications.

It is the responsibility of the trial monitor to:

- Provide sites with contact details of all monitors involved in the multi-site submission process
- Provide the CPI with contact information for participating sites (PI details and their nominated site contact person)
- Provide all participating sites with CPI site contact information (CPI details and their nominated site contact person)
- Notify the CPI of changes in participating site contacts
- Notify the CPI and participating sites of any changes to sponsor/CRO staff
- Keep distribution lists up to date to ensure staff are included in information flow
- Maintain a master contact list for sites
- Confirm the ethics submission meets all state-specific and legislative requirements
- Prepare a preliminary document package for parallel submission of research governance/SSA documents to the RGO of participating sites. Initial documents include but are not limited to indemnity, insurance certificate of currency, protocol, investigator brochure and draft budget.

Although most information is provided to the RGO via the site personnel, the monitor should obtain contact details for relevant RGO personnel at each participating institution.

Each site is responsible for informing the sponsor/CRO of any site changes. A master contact list should be maintained and provided to the monitor on a regular basis or as required.

6.2.2 Trial master files

Trial master files should be part of the initial communication plan and discussions. The CPI and participating sites should discuss the following with the trial monitor:

- Targeted timelines for each of the listed documents
- Who is responsible for the provision and review of the documents (see *Roles and Responsibilities in a Research Project* at www.clinicaltrialsandresearch.vic.gov.au/ethics-application)
- Nomination of back-up individuals within each institution in the event of absent staff.

6.2.3 ERM and SSA

ERM (https://au.forms.ethicalreviewmanager.com) is used for all ethics and research governance/SSA applications in Victoria and Queensland.

ERM allows document management and information sharing between the sponsor/CRO, CPI and PIs. It is used for completion and submission of the ethics application to the reviewing HREC, and completion and submission of SSAs to the RGO for each site. ERM is also used for communication with the reviewing HREC or RGO following submission, including notification of approval/authorisation.

In order to maximise efficiency of ethics and research governance/SSA processes, the sponsor/CRO should be familiar with the features and use of ERM. Information and training are at www.clinicaltrialsandresearch.vic.gov.au/ethical-review-manager.

Once site selection has occurred the sponsor/CRO, in conjunction with sites, should establish a plan for responsibilities in ERM (see Appendix 3).

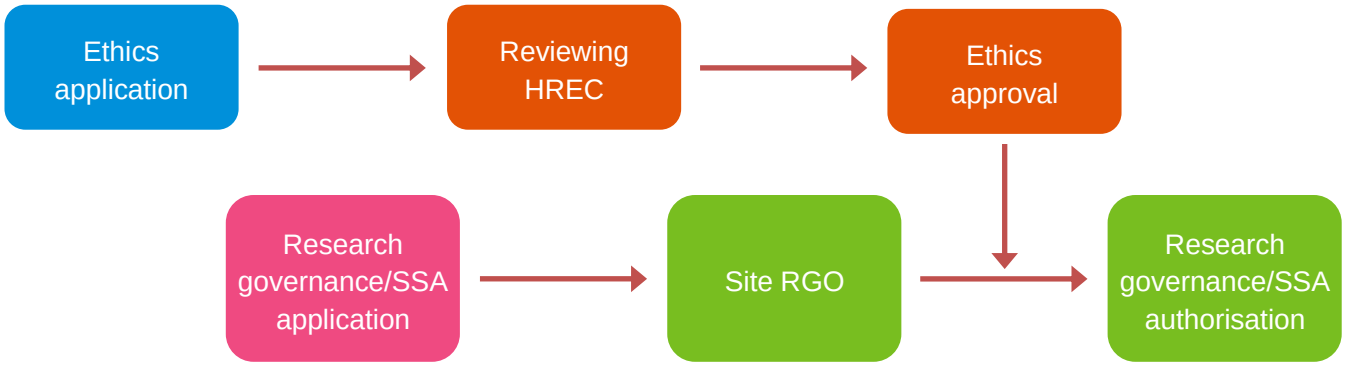
The sponsor should be given access to the SSA in ERM by either the project owner or SSA owner. For guidance, refer to the Applicant User Guide to ERM.

Information on systems for SSAs for other states/territories is at www.clinicaltrialsandresearch.vic.gov.au/national-mutual-acceptance.

6.2.4 Parallel submission to the HREC and RGO

The sponsor/CRO should ensure that both HREC and research governance/SSA site-specific documents are prepared and ready for submission. In ERM, the SSA and its supporting documents can be submitted to the RGO as soon as the ethics application is submitted.

The recommended practice is to submit the SSA, with as many supporting documents as possible, to the site RGO as soon as the ethics application is submitted to the reviewing HREC. Some documents (e.g. research agreement) may require thorough and lengthy review, and providing these early allows the RGO time to perform the institution's review without delaying SSA authorisation. Some documents are provided to the RGO at a later date (e.g. HREC approval letter) but should not hold up the initial SSA submission and assessment process.



The sponsor/CRO should:

- Review institutional websites prior to SSA submission to ensure any site-specific requirements are addressed
- Prepare a set of pre-HREC approval documents to be submitted to the RGO as early as possible.

There will be follow-up documents provided to the RGO upon HREC approval but this should not hold up the initial SSA submission and assessment process. These follow-up documents can be provided to the RGO immediately after notification of approval.

The monitor should confirm the documents and versions are correct before submission to the RGO. The document versions uploaded into ERM are reviewed by the RGO, and they will be listed on the authorisation letter. It is imperative that the correct version is included and any superseded versions are removed from the submission. For guidance, refer to Section 10 of the Applicant User Guide to ERM.

The PI/trial coordinator completes the SSA form on ERM, but it is recommended that the sponsor/CRO provides generic text. This assists with completion of the SSA form and avoids additional work where multiple sites are involved. During the SSA preparation process, the site may request additional information from the sponsor/CRO. It is recommended that responses are provided within five working days.

The PI/trial coordinator uses ERM to submit the signed SSA and supporting documents to the site RGO. The RGO then uses ERM to review the application and request additional information from the PI, if required. The

PI may contact the sponsor/CRO to source the information, and the sponsor/CRO must provide it in a timely manner to ensure efficient review of the SSA.

If the PI does not respond to a RGO's request within four weeks, the sponsor/CRO could consider making direct contact with the RGO.

Tracking the progress of the ethics and research governance/SSA applications from submission to approval/authorisation can be managed efficiently in ERM using the History and Submissions tabs. Refer to Section 2.7 of the Applicant User Guide to ERM.

6.2.5 Authorisation

When the RGO is satisfied the SSA application meets all requirements, they authorise it and notify the site PI/trial coordinator via ERM.

The RGO issues an approval letter via ERM, which lists the current versions of supporting documents submitted.

The site PI/trial coordinator forwards the authorisation letter to the sponsor/CRO. Alternatively, if the sponsor/CRO has a role with permission to view communications in ERM, they can access the letter themselves.

The timeline for SSA authorisation is dependent on relevant site documents being submitted to the RGO and assessed prior to receipt of HREC approval. The RGO should notify the PI of SSA authorisation within one day of the decision.

For the duration of the project, the RGO must be provided with all relevant amendments, notification of HREC approval of amendments, and any information relevant to the conduct of the project.

6.3 During the research project

For the duration of an approved research project, the reviewing HREC is responsible for monitoring the ethical conduct and safety of the research. The site RGO is responsible for monitoring the conduct of the research project at a site. The CPI, PI and sponsor/CRO have ongoing responsibilities to report to the HREC and RGO.

Information on reporting is at www.clinicaltrialsandresearch.vic.gov.au/monitoring-and-reporting.

Reporting to a Victorian site RGO is managed in ERM; see Section 15 of the Applicant User Guide to ERM.

A communication plan should identify items that must be reported throughout the course of the research, with agreed timelines for communication and document provision among the parties. The communication plan assists sites and trial monitors to effectively manage the ongoing activities of the research. This may involve telephone, emails, remote and onsite monitoring activities, newsletters, follow-up letters and project-specific web portals.

Reporting to the HREC and RGO is managed in ERM and is generally the responsibility of investigators (refer to Section 4.3 for information), although safety reporting falls to the sponsor/CRO. The sponsor/CRO can assist with creating and completing reports as appropriate. Responsibilities for reporting should be established at the inception of the research project (Appendix 3 can assist).

Use the collaboration features of ERM for efficiency in reporting processes. With an appropriate role in ERM, the sponsor/CRO can view all reporting information and communications

6.3.1 Amendment

An amendment is a written change to an HREC-approved protocol for ongoing research. The reviewing HREC is responsible for review and approval of an ethics amendment, and the site RGO must also authorise the amendment before it can be implemented at the site.

6.3.1.1 Notify the RGO of an ethics amendment

The CPI/trial coordinator is responsible for submitting an amendment request to the reviewing HREC. For a HREC in Victoria, an *Ethics Amendment Request* form is created as a sub-form of the HREA in ERM. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for approval.

The CPI or sponsor/CRO must notify participating site PIs of the ethics amendment and its approval. The communication preference should be clearly established at the beginning of the research project, to ensure all relevant HREC-related information and correspondence is distributed to participating sites.

Any change to the ethically approved project can impact SSA authorisation, and so the RGO must be notified in a timely manner.

When the site PI/trial coordinator receives information about an ethics amendment, they create a *Site Governance Amendment Request* form as a sub-form of the SSA in ERM. Supporting documents are uploaded and it is submitted to the RGO. The RGO assesses the amendment and makes an authorisation decision.

The RGO notifies the PI of amendment authorisation, and this should be shared with the sponsor/CRO (who can also access the authorisation information in ERM, if given appropriate role).

6.3.1.2 Local research governance/SSA amendment

Local changes to site conduct of a research project may require only a research governance amendment, and not need ethics approval. For example, addition of a new Associate Investigator would be a site governance issue. In general, the site PI is responsible for this type of amendment (refer to Section 4.3.1.2) and the sponsor/CRO may have little procedural involvement. The PI should notify the sponsor/CRO of the change.

6.3.2 Safety report

All safety reporting must align with the NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*, in which safety monitoring and reporting to the reviewing HREC is assigned to the sponsor of the research project. Some types of safety event require time-critical reporting, and the CPI or PI may action reporting where appropriate. Some HRECs or RGOs may require the CPI or PI to review safety reports before they are submitted, and local regulations must be followed.

The sponsor/CRO should:

- Ensure the trial protocol has clear sections describing:
  - The assessment and management of risk (if not in an alternative document)
  - Safety reporting definitions, procedures, responsibilities and reporting timelines
  - Any serious adverse events that do not require immediate reporting
- Keep detailed records of all reported adverse events and maintain up-to-date tabulations and/or line listings
- When communicating safety information to investigators and/or HRECs, clarify the impact of each report on patient safety, trial conduct or trial documentation

- Assess and categorise the safety reports received from investigators, and report all SUSARs or USADEs occurring in Australian participants to the Therapeutic Goods Administration
  - For fatal or life threatening Australian SUSARs or USADEs, immediately, but no later than 7 calendar days after being made aware of the case, with any follow-up information within a further 8 calendar days
  - For all other Australian SUSARs or USADEs, no later than 15 calendar days after being made aware of the case
- Review the investigator's brochure at least annually and update it when new and relevant information becomes available
- Provide the HREC and investigators with any update/addenda of the investigator's brochure or where applicable, Product Information
- Provide the HREC with an annual safety report including a clear summary of the evolving safety profile of the trial. This report should allow the HRECs to assess whether ongoing safety monitoring is being conducted appropriately and the trial's safety monitoring plans are being followed and where necessary, are being adapted to take into account new findings as the trial progresses
- Ensure all sponsor responsibilities for safety monitoring and reporting (e.g. reporting SUSARs and significant safety issues to the TGA) are appropriately allocated or delegated
- Notify the TGA, HREC and investigators of all significant safety issues that adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial. Significant safety issues that meet the definition of an urgent safety measure should be notified within 72 hours, and all other significant safety issues should be notified within 15 calendar days of the sponsor instigating or being made aware of the issue.

A safety event must be notified to the reviewing HREC. For reporting to a HREC in Victoria, a *Safety Report* is created as a sub-form of the HREA in ERM. Supporting documents are uploaded to the report and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt, and may provide instruction.

The sponsor/CRO or CPI notifies the site PI of the event and the HREC's response, and the PI notifies the site RGO via ERM. The PI creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt, and may provide instruction.

The site (institution) bears the legal liability for participants. In an instance of a high-risk safety event, the institution could suspend or close the research project at the site. Suspension can later be lifted if the RGO is satisfied the risk has been mitigated.

In the event of a SUSAR or USADE at a site in Victoria, VMIA must be notified by the institution.

6.3.2.1 Annual safety report

An annual safety report is required for an interventional clinical trial, in line with NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*. The timing of the annual safety report is at the discretion of the reviewing HREC; they may specify a date or it may align with the sponsor/CRO's reporting cycle. Consult the reviewing HREC's website for information.

For reporting to a HREC in Victoria, an *Annual Safety Report* is created as a sub-form of the HREA in ERM. Supporting documents (e.g. sponsor/CRO global safety information) can be uploaded to the report and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt.

The PI notifies the site RGO via ERM. The PI/trial coordinator creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents (including a copy of the *Annual Safety Report*) are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt.

6.3.3 Breach report

Breach reporting must align with NHMRC's *Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods*. The sponsor/CRO must familiarise themselves with this guidance, in order to meet their reporting obligations.

The sponsor/CRO should:

- Develop documented processes for managing serious breaches including:
  - Assessment of whether the serious breach is isolated or systemic
  - Assessment of the impact of the serious breach on participants and on the reliability and robustness of trial data
  - Investigation procedure
  - Reporting procedure
  - Management of corrective and preventative action (CAPA)
  - Circulation and retention of documents relating to serious breaches.
- Report serious breaches to the reviewing HREC within 7 calendar days of confirming a serious breach has occurred and provide follow-up reports when required
- For serious breaches occurring at a trial site, notify the site's principal investigator within 7 calendar days of confirming a serious breach has occurred
- Perform a root cause analysis and ensure appropriate corrective and preventative actions are taken
- Where the sponsor determines a third party report, provided to it by the HREC, meets the definition of a serious breach, report the serious breach to the reviewing HREC within 7 calendar days of this decision.

A serious breach must be notified to the reviewing HREC. In Victoria, a *Serious Breach Report* is created as a sub-form of the HREA in ERM. Supporting documents are uploaded and it is submitted to the reviewing HREC, who assess the information and acknowledge receipt. The CPI or PI may report a suspected breach using the *Suspected Breach Report* and following the same process.

The CPI or sponsor/CRO notifies the site PI of the breach and the HREC's response, and the PI notifies the site RGO via ERM. The PI/trial coordinator creates a *Site Notification Form* as a sub-form of the SSA in ERM. Supporting documents are uploaded to the sub-form and it is submitted to the RGO. The RGO assesses the information and acknowledges receipt.

A non-serious breach occurring at a site may be notified to the RGO, at their discretion. The site PI should discuss a possible non-serious breach with the RGO to determine if reporting is required. The PI reporting process is in Section 4.3.3.

6.3.4 Progress reports

Information on the progress of an approved research project must be provided to the reviewing HREC in accordance with NHMRC's *National Statement on Ethical Conduct in Human Research*.

The schedule for reporting on a project is determined by the reviewing HREC and RGOs. The frequency of reporting is detailed in the ethics approval letter and research governance/SSA authorisation letter.

The CPI is responsible for reporting to the reviewing HREC for all approved sites. To compile a progress report for a multi-site project, the CPI/trial coordinator or sponsor/CRO gather information from all site PIs/trial coordinators. It should be determined at the commencement of the project who is responsible for gathering and collating the information. This data collection should be done well in advance of the report due date. Each site PI/trial coordinator must supply their information in a timely manner to allow reporting obligations for the project to be fulfilled.

For a HREC in Victoria, the CPI/trial coordinator creates a *Project Progress Report* as a sub-form of the HREA in ERM. Aggregate information for all sites approved by the HREC is included in the report. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for review and acknowledgement.

The site PI is responsible for reporting to the RGO regarding progress at their site, in line with site policy. The PI/trial coordinator creates a *Site Progress Report* as a sub-form of the SSA in ERM. Supporting documents can be uploaded to the report and it is submitted to the RGO. The RGO reviews the report and acknowledges receipt.

6.3.5 Closure

The reviewing HREC must be notified by the CPI when a research project closes, or when a site closes from an ongoing multi-site project. The RGO must be informed when their own site closes.

If one site closes from a multi-site project that is continuing at other sites approved by a Victorian HREC, the CPI/trial coordinator creates a *Site Closure Report* as a sub-form of the HREA in ERM. When the research project is completed at all sites approved by a Victorian reviewing HREC, the CPI/trial coordinator creates a *Project Final Report* as a sub-form of the HREA in ERM. Supporting documents can be uploaded to the report and it is submitted to the reviewing HREC for review and acknowledgement. The research office must record the project as '**Closed**' in ERM.

The site PI is responsible for reporting to the RGO regarding site closure or project completion. The PI/trial coordinator creates a *Site Progress Report* as a sub-form of the SSA in ERM. Supporting documents are uploaded and it is submitted to the RGO. The RGO reviews the report and acknowledges receipt. The RGO records the research governance/SSA record '**Closed**' in ERM.

When the clinical trial has been completed at all approved sites, the sponsor/CRO should notify the TGA of trial completion. The CTN is used to submit completion advice to the TGA.

6.3.6 Other post-authorisation reports

A *Site Audit Report, Complaint Report* and *Site Notification Form* are available in ERM for reporting to the site RGO. The RGO directs the PI regarding when these forms are required, and the PI completes and submits the form to the RGO. The PI may require information from the sponsor/CRO for input into the form; the sponsor/CRO should provide the information promptly to avoid causing any delay.

7 Summary

	Getting started	Research governance/ SSA application	During the research project	Closure
Coordinating Principal Investigator or trial coordinator or trial coordinator	With sponsor/CRO, identify: • PI/trial coordinator at each site • RGO at each site • trial monitor Develop: • contact template • ERM delegation list	In ERM (or may be done by sponsor/CRO): • Give site PI a role to view ethics application and its supporting documents • Create SSA for each site, or give PI role to create their own SSA • Transfer SSA to PI Provide site PI a copy of ethics approval letter	For progress report to reviewing HREC, collate site information from all PIs. Submit all post-approval (ethics) reports (e.g. safety, amendment, progress report) to reviewing HREC. Following all post-approval reporting, provide copy to site PI for submission to RGO.	If 1 site closing from multi-site project, submit site closure report to reviewing HREC. For final report to reviewing HREC, collate site information from all PIs and submit to reviewing HREC. Following all post-approval reporting, provide copy to site PI for submission to RGO.
Site Principal Investigator or trial coordinator	Verify research team and SSA signatories have ERM accounts and are familiar with its use.	Quality check all SSA supporting documents. Complete, sign and submit SSA to RGO. If requested to provide more information by RGO, edit SSA and/or supporting documents; verify that only current document versions are included; resubmit in a timely manner.	When requested, provide site progress information promptly to CPI for inclusion in project progress report. Complete, sign, submit post-authorisation reports to RGO; include copy of post-approval (ethics) report. Liaise with RGO, CPI, and sponsor/CRO about site safety event.	Provide site information to CPI for inclusion in report to HREC. Complete, sign, submit post-authorisation reports (closure/final) to RGO; include copy of post-approval (ethics) report.
Site Research Governance Officer	Advise site PI/trial coordinator and sponsor/CRO of site requirements for research governance/SSA.	SSA supporting document quality check. Assess all documents including HREC-related and SSA. Process SSA in ERM: • If applicable, record 'partial application', request information from PI/trial coordinator. • Authorise SSA, notify PI/trial coordinator.	Liaise with PI/trial coordinator re post-authorisation reporting. Review post-authorisation reports, assess for implications on the site and record decisions in ERM. Notify PI/trial coordinator of post-authorisation decisions. Perform research audit.	Review post-authorisation reports (closure/final) and process in ERM. Acknowledge report to PI/trial coordinator. Close SSA in ERM.
Sponsor or Contract Research Organisation	With CPI, identify: • PI at each site • RGO at each site • trial monitor Provide sites with: • protocol • investigator brochure • master PICF Obtains site details for: • legal documents Communication plan: • site liaison persons	In ERM (or may be done by CPI: • Give site PI a role to view ethics application and its supporting documents • Create SSA for each site, or give PI role to create their own SSA • Transfer SSA to PI Document and quality checks	Liaise with site research teams. Report safety events and breaches to reviewing HREC via post-approval reporting. Contribute to post-authorisation reporting as required.	In ERM, view the post-approval and post-authorisation reports (closure/final) and HREC and RGO responses.

8 Acknowledgements

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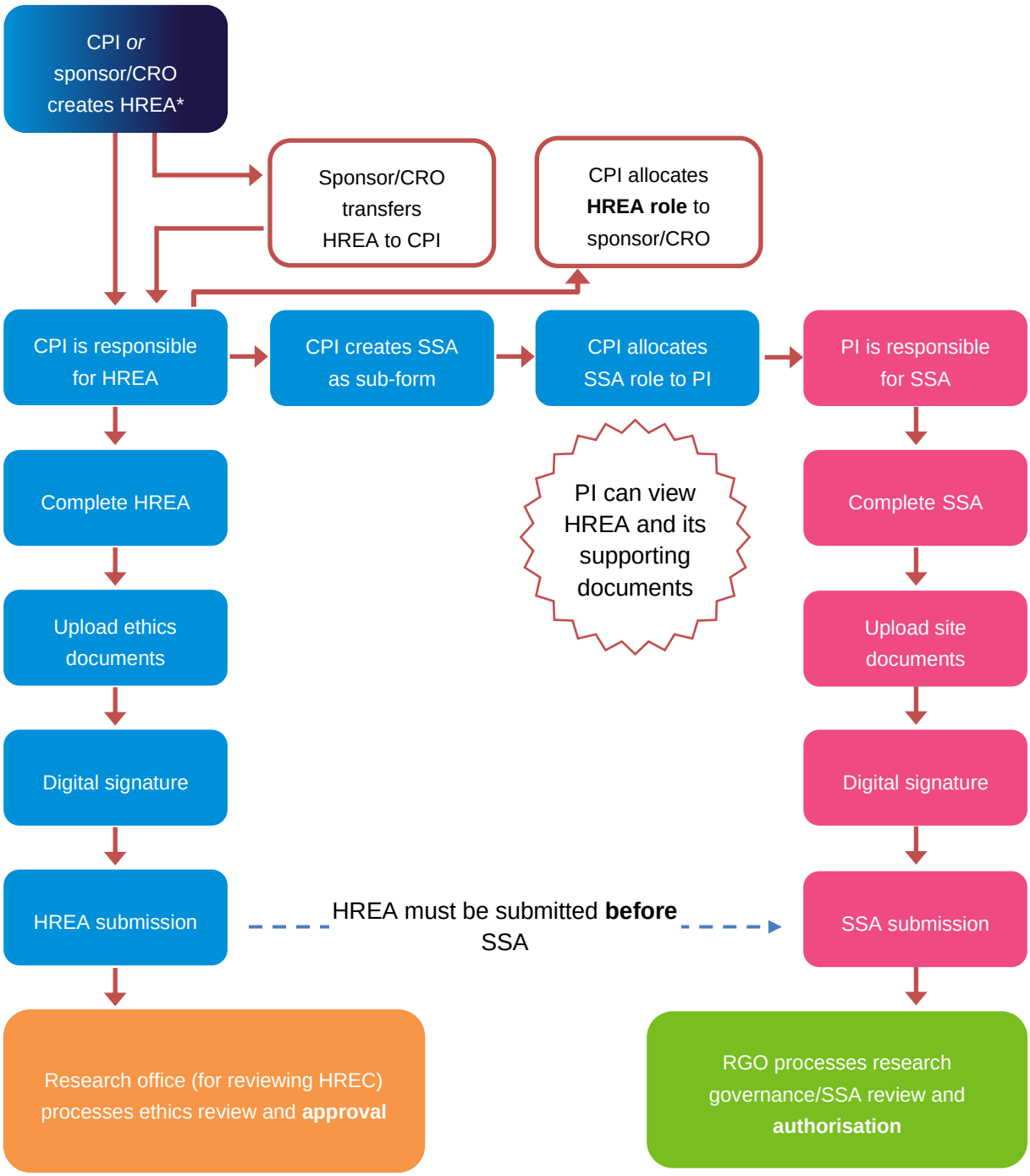
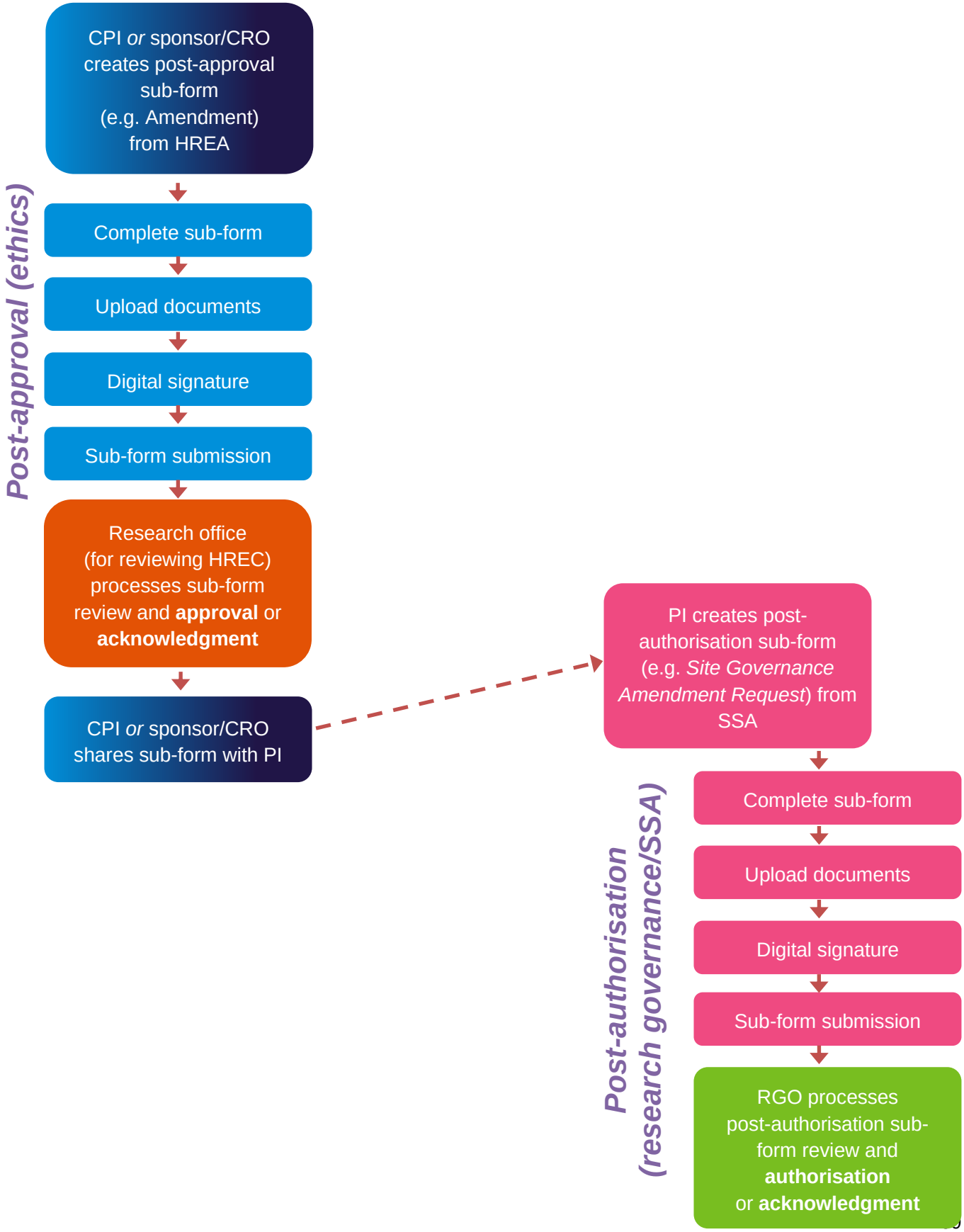
This 2022 version of *Research Governance and Site Specific Assessment – Process and Practice* has been updated by the Coordinating Office for Clinical Trial Research, Victorian Department of Health. Expert review was carried out by subject matter experts. Those who have contributed to this version are acknowledged and thanked for their time.

Appendix 1: Ethics and research governance/SSA



* For a NMA project with ethical review outside Victoria or Queensland, a **MDF** is created instead of a HREA. The process is the same, except signature is not required on the MDF and it does not go through an *approval* process.

Appendix 2: Post-approval and post-authorisation



Appendix 3: ERM delegation for multi-site project

Use this checklist at commencement of a research project to record the parties responsible for ERM tasks. The CPI and site PI may delegate some responsibilities to a member of the research team (e.g. trial coordinator).

Stage	Task	Sponsor /CRO	CPI	Site PI
Preparation	Has ERM account	☐	☐	☐
	Has access to Applicant User Guide to ERM	☐	☐	☐
	Has attended/viewed ERM training	☐	☐	☐
	Will be ERM project owner (has full access permissions)	☐	☐	
Ethics review in VIC or QLD	Create HREA	☐	☐	
	Create VSM (sub-form of HREA)	☐	☐	
	Complete HREA	☐	☐	
	Complete VSM	☐	☐	
	Upload supporting documents (including VSM) to HREA	☐	☐	
	Record project is NMA *if applicable*	☐	☐	
	Request HREA signature(s) *if applicable*	☐	☐	
	Sign HREA		☑	☐
	Submit HREA		☑	
	Submit VSM		☑	
	Resubmit in response to query or information request from HREC		☑	
	Monitor HREC review progress using History tab	☐	☐	
	Assign each VIC and QLD site PI a role to access HREA HREA role assigned to each site PI: *Recommended* → Read, create sub-forms ☐ Read only ☐ Read, write ☐ Read, write, submit ☐	☐	☐	
If NMA ethics review is outside	Create MDF (once only for the project)	☐	☐	
	Complete MDF	☐	☐	
	Upload ethics documents to MDF	☐	☐	
	Submit MDF	☐	☐	

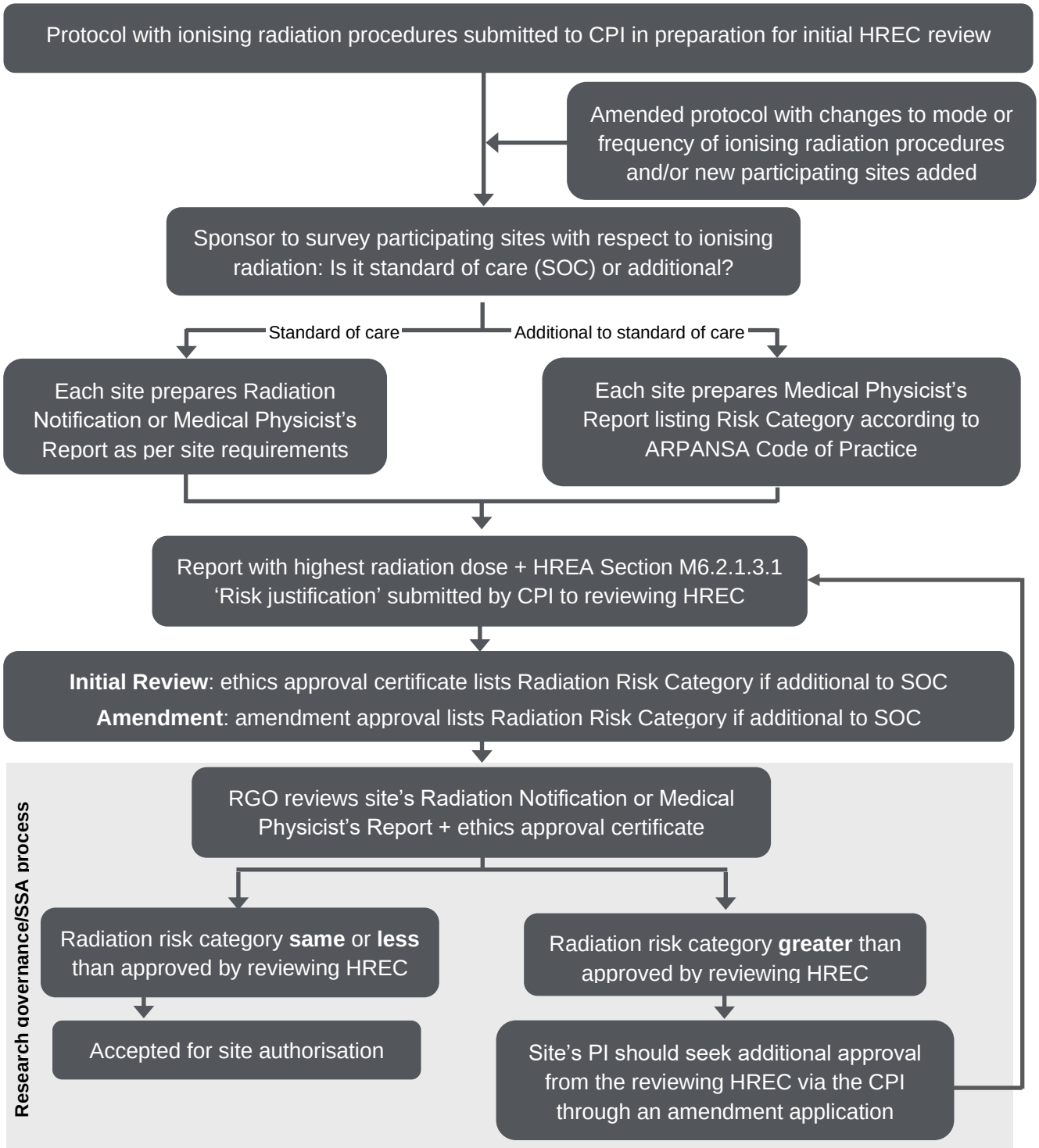
Stage	Task	Sponsor /CRO	CPI	Site PI
VIC or QLD	Assign each VIC and QLD site PI a role to access MDF	☐	☐	
Research governance /SSA	Create SSA (must be HREA/MDF owner or have suitable role)	☐	☐	☐
	Transfer SSA to new owner *if applicable*	☐	☐	☐
	Assign site research team members a role to access SSA	☐	CPI is PI for their own site.	☐
	Complete SSA			☑
	Upload supporting documents to SSA			☑
	Request SSA signature(s)			☑
	Sign SSA			☑
	Submit SSA			☑
	Resubmit in response to information request from RGO			☑
	Monitor RGO review progress using History tab	☐		☐
Post-approval reporting to VIC HREC	Create post-approval form (must be HREA owner or have suitable role)	☐	☐	PI may action urgent safety reporting if sponsor/CRO and CPI unavailable.
	Complete post-approval form	☐	☐	
	Upload supporting documents to post-approval form *if applicable*	☐	☐	
	Sign post-approval form	☐*	☐	
	Submit post-approval form	☐*	☐	
	Resubmit in response to information request from HREC	☐*	☐	
	Monitor HREC review progress using History tab	☐	☐	
	Assign each VIC site PI a role to access the post-approval form	☐	☐	
Post-authorisation reporting to VIC RGO	Create post-authorisation form (must be SSA owner or have suitable role)	☐	☐	☐
	Transfer post-authorisation form to site PI *if applicable*	☐	☐	
	Assign site research team members a role to access post-authorisation form	☐	CPI is PI for their own site.	☐
	Complete post-authorisation form			☑
	Upload supporting documents to post-authorisation form			☑
	Request post-authorisation form signature(s) *if applicable*			☑
	Sign post-authorisation form			☑

Stage	Task	Sponsor /CRO	CPI	Site PI
	Submit post-authorisation form			☑
	Resubmit in response to information request from RGO			☑
	Monitor RGO review progress using History tab	☐		☐

* Sponsor/CRO may sign and submit a **safety** or **breach** report in line with NHMRC's *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* and *Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods*. All other post-approval forms should be signed and submitted by the CPI. **Parties must adhere to the reviewing HREC's policy on signatories.**

Appendix 4: Ionising radiation

If a research project involves exposing participants to ionising radiation, specific regulatory requirements and supporting documents are required. Flow diagram developed by *Victorian Hospital Medical Physicists*.



Appendix 5: Contacts for multi-site project

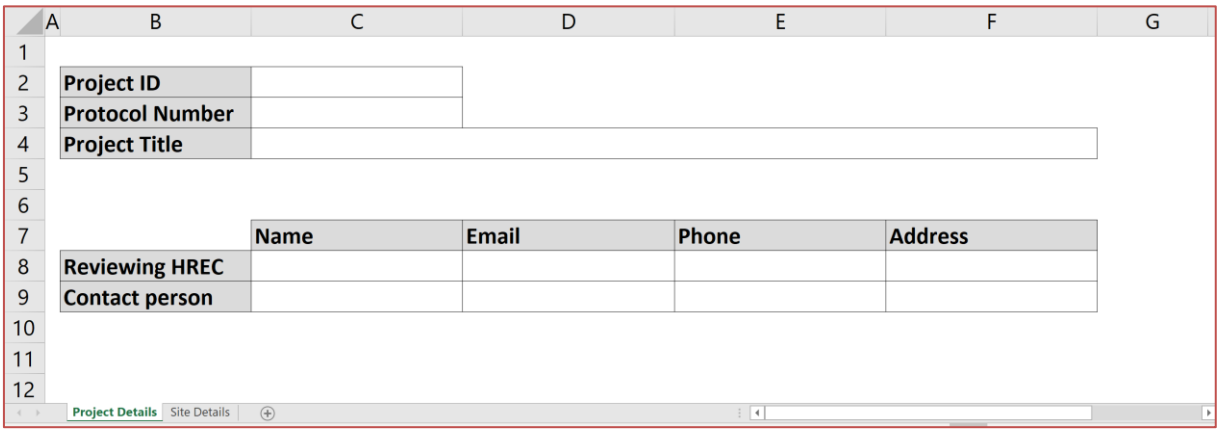
It is recommended to use a spreadsheet to capture contact details for all sites participating in a multi-site project.

Excel template:

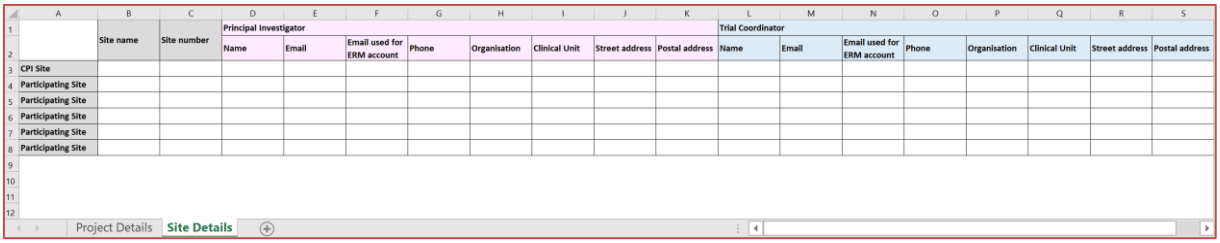
ContactListTemplate.xlsx

The Excel template link may not operate if viewing this document as a PDF. A Microsoft Word version of this document, along with the Excel template, is at www.clinicaltrialsandresearch.vic.gov.au/research-governance-applications. Alternatively, create a new spreadsheet using the suggested layout below.

Project details tab



Site details tab



Appendix 6: Research agreement checklist

Use this checklist for completion and review of a research agreement.
Adapted from Alfred Health 'Non Investigator Initiated Checklist'.

Part 1: Select the type of research agreement used for the project.

Type of research	Research agreement	
Teletrial	CTRA subcontract for studies conducted under a tele-trials model* • ***Must also select another research agreement from this list.*** • ***The checklist in Part 2 below does not apply for a tele-trials subcontract.***	☐
Clinical trial of a drug	CTRA – Medicines Australia Standard Form	☐
	CTRA – CRO acting as the local sponsor	☐
	CTRA – Collaborative or Cooperative Research Group (CRG) studies	☐
	CTRA – Phase 4 clinical trial (medicines)	☐
	CTRA – Phase 4 clinical trial (medicines) CRO acting as the local sponsor	☐
Clinical trial of a device	MTAA Standard CIRA	☐
	MTAA Standard CIRA Post Market	☐
	MTAA CIRA: Contract Research Organisation acting as the Local Sponsor	☐
	MTAA CIRA: Post Market Clinical Trial (Medical Devices) – Contract Research Organisation acting as Local Sponsor.	☐
Investigator initiated	Investigator initiated CTRA	☐
Any	Non-standard research agreement • ***Legal review is advised; consult institution's website or contact RGO.*** • ***Do not complete the checklist in Part 2 below.***	☐

* Agreement between the primary site and satellite site; required for each teletrial satellite site, in addition to the CTRA (head agreement) between the sponsor and primary site.

Part 2: Complete the checklist

Section of CTRA or CIRA	Checklist item	Yes	No	N/A
Details of the parties	Are the institution name, ABN and address correct?	☐		
	Is the sponsor/CRG the same as that named on the CTN?	☐		☐
	Are the sponsor/CRG full legal name, ABN and address correct?	☐		

Section of CTRA or CIRA	Checklist item	Yes	No	N/A
	Are the study name and protocol number correct?	☐		
	Is the *Date of Agreement* **blank**? • *The date is recorded when the last party signs.*	☐		
Key information	Are the *Study Name* and local *Study Site* details correct?	☐		
	Is the *Target Number of Study Participants* the same as stated on the ethics and/or research governance/SSA application?	☐		
	Are the *Recruitment Period* dates correct?	☐		
	Is the *Reviewing HREC* name correct?	☐		
	Is all *Equipment Provided by Sponsor* listed?	☐		☐
	Is the listed *Equipment Provided by Sponsor* approved by the TGA?	☐	☐	☐
	Is *Equipment Provided by Sponsor* sourced from the Australian Sponsor as defined on the ARTG?	☐	☐	☐
	If equipment is **not** approved by the TGA and/or **not** sourced from the Australian sponsor, is it listed on the CTN?	☐		☐
Payments	Are the terms and conditions of payment satisfactory?	☐		
	Are the amounts exclusive of GST? • *If amount includes GST, the actual amount received will be less than that.*	☐		
	Are the amounts satisfactory? • *Amounts must cover costs outlined in department declarations*	☐		
	Is the currency Australian dollars?	☐	☐	
	If the currency is not Australian dollars, are the converted amounts satisfactory?	☐		☐
	Will a start-up fee be paid if a pre-nup has not been signed?	☐		☐
	Is the research team able to comply with any requirements to complete case report forms (CRFs) within a specified period?	☐		☐
	Is the research team able to meet participant enrolment timelines?	☐		☐
	Is the research team satisfied with the definition of 'screen failure' and the capped number of screen failures?	☐		☐
	Will the research team be reimbursed for work associated with preparation of any future amendment	☐	☐	

Section of CTRA or CIRA	Checklist item	Yes	No	N/A
	applications, safety reports, progress reports, meetings etc?			
	Have any bonus payments been offered which could be considered an inducement to enrol additional participants?	☐	☐	
	Have archiving costs been included in the payment amounts?	☐	☐	
	Is a third party making payments on behalf of the local sponsor? • *Research team **must not** follow-up on overdue payments from a third party. Local sponsor is responsible for payment being made.*	☐	☐	
	Are there any terms which the research team are unsure about? • *If yes, contact the institution's RGO.*	☐	☐	
	Are the account details complete and correct?	☐		
Form of indemnity for clinical trials*	Is an unsigned indemnity inserted?	☐		☐
Insurance arrangements*	Is a current insurance certificate, complying with the minimum requirements, inserted? • *Check the certificate expiry date to verify it is current.*	☐		☐
Guidelines for compensation for injury resulting from participation in a company-sponsored trial*	Have the *Guidelines for Compensation* been attached or a link to them on the Medicines Australia or Medicine Technology Association of Australia website provided?	☐		☐
Study protocol identification ***OR*** Clinical investigation plan identification	Are all details correct?	☐		
Special conditions	Is *only* SEBS-endorsed wording included? • *Wording must either be endorsed by SEBS or reviewed by the institution's legal counsel. Legal review may incur a fee.* • *If the third party beneficiary clause is included, it must be endorsed by SEBS for the particular sponsor.*	☐		

* Section is not present in some CTRA and CIRA templates. Record N/A if section is not applicable.

Appendix 7: Indemnity checklist

Use this checklist for completion and review of indemnity documents.
Adapted from Alfred Health 'Non Investigator Initiated Checklist'.

Part 1: Standard Form of Indemnity

Section of Standard Form of Indemnity	Checklist item	Yes	No
To clause	Is the institution defined as "the Indemnified Party"?	☐	
	Are the institution's name and ABN correct?	☐	
From clause	Is the sponsor defined as "the Sponsor"?	☐	
	Are the sponsor's full legal name and ABN correct?	☐	
Re clause	Are the study title and protocol number (or clinical investigation plan details) correct?	☐	
Paragraph 1	Is the correct cohort selected as "the Participants"? 〉 *Options are: patients of the Indemnified Party; non-patient volunteers.*	☐	
	Is the correct name of the Principal Investigator recorded for "the Investigator"?	☐	
	Is the indemnity defined as "Schedule 3" or "Exhibit X"? 〉 *The signed indemnity must be separate from the CTRA/CIRA.*		☐

To receive this document in another format, phone 0408 274 054, using the National Relay Service 13 36 77 if required, or email Coordinating Office for Clinical Trial Research <multisite.ethics@health.vic.gov.au>

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